

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

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Certified American Board of Ophthalmology

Ballantrae Community Zoom presentation 4 Feb 2021

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

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

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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

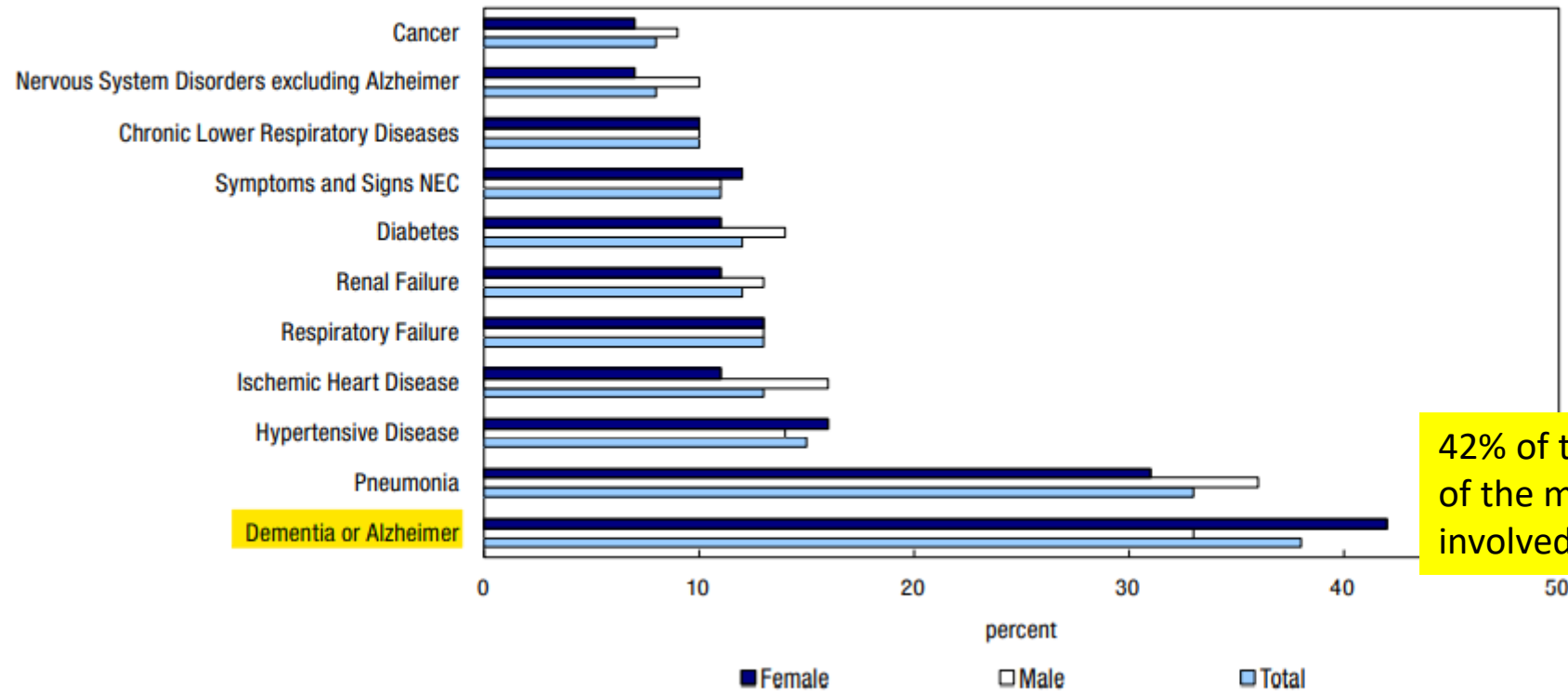
Statistique
Canada

Canada

Chart 1

Common medical conditions or complications (comorbidities) associated with a severe course of COVID-19 resulting in death, by sex

Common COVID-19 comorbidities



42% of the women and one-third of the men (33%) in COVID-involved deaths (Dementia)

Note: Comorbidities for deaths occurring between March 1, 2020 and July 31, 2020, where COVID-19 was involved.

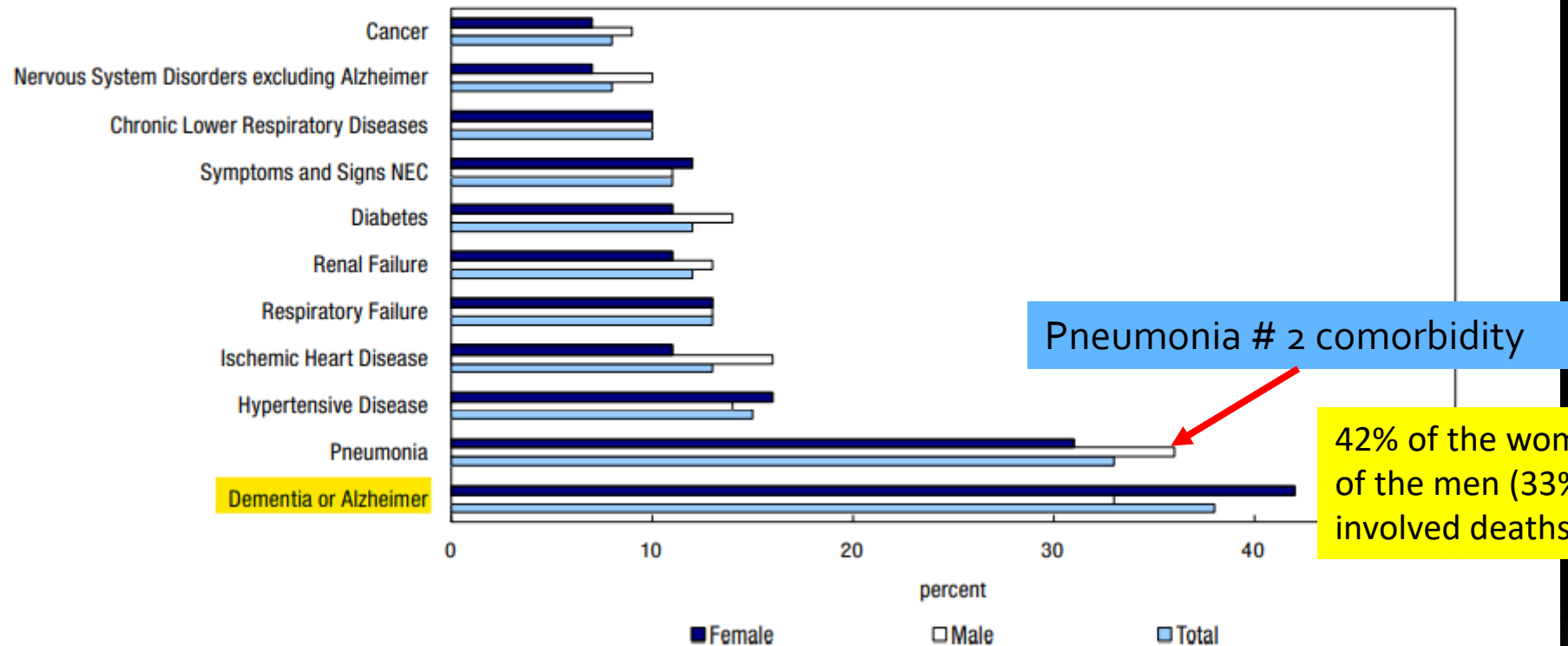
Source: Canadian Vital Statistics – Death Database (2020).

1. Government of Canada. 2020. <https://www.canada.ca/en/public-health/services/publications/diseases-conditions/people-high-risk-for-severe-illness-covid-19.html>; See also Centers for Disease Control and Prevention. 2020. Evidence used to update the list of underlying medical conditions that increase a person's risk of severe illness from COVID-19. <https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/evidence-table.html>.
2. Weekly report of the United States' National Center for Health Statistics on COVID-involved mortality. https://www.cdc.gov/nchs/nvss/vsrr/covid_weekly/index.htm.

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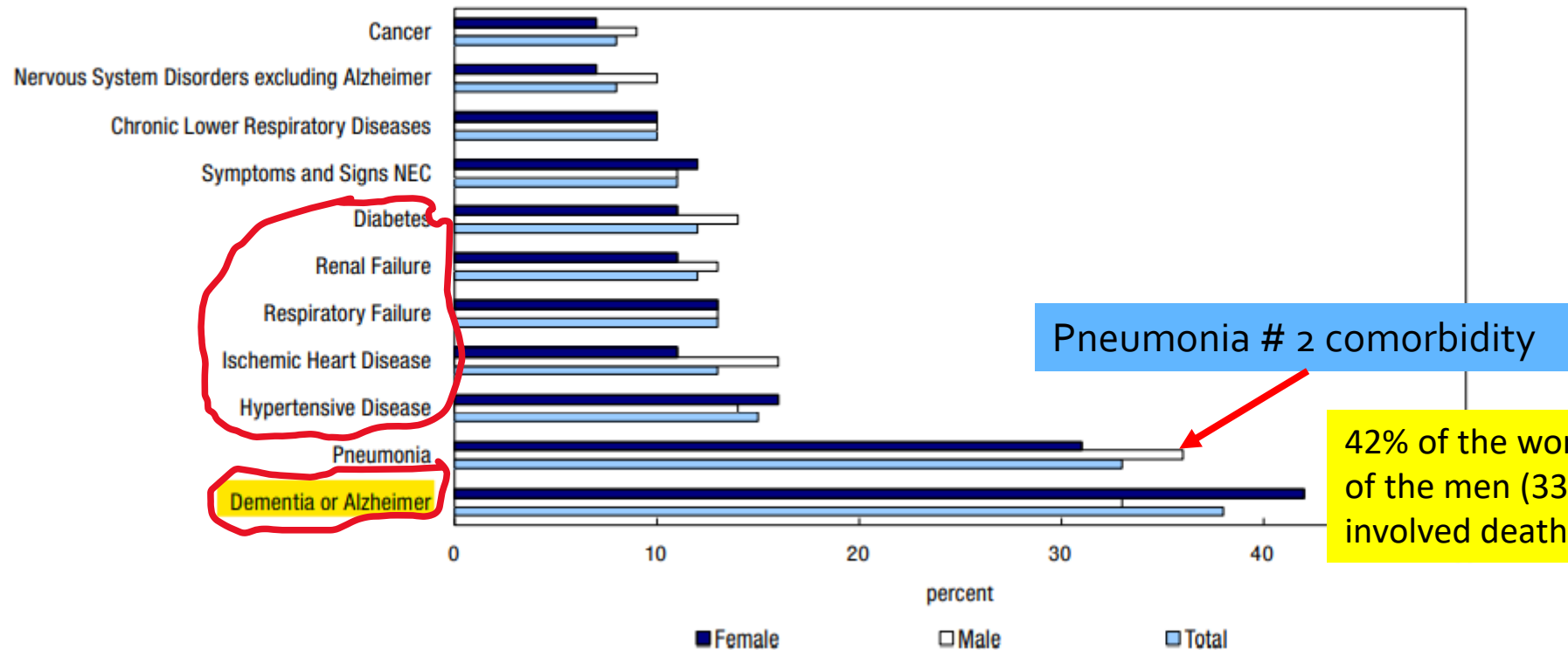
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INTERNATIONAL
SOCIETY
FOR INFECTIOUS
DISEASES

Review

Comorbidities and the risk of severe or fatal outcomes associated with coronavirus disease 2019: A systematic review and meta-analysis

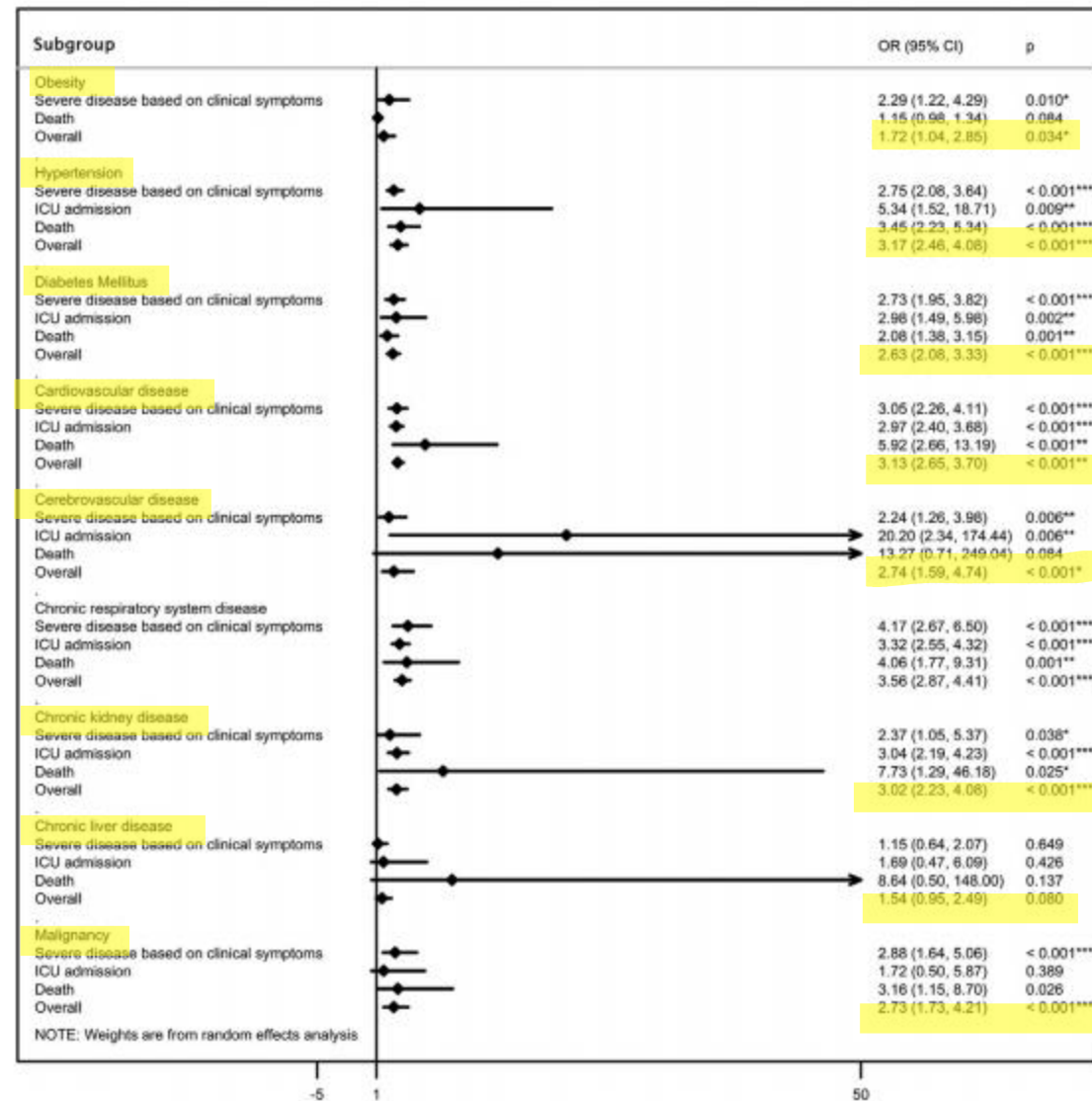


Yue Zhou^a, Qing Yang^b, Jingwei Chi^a, Bingzi Dong^a, Wenshan Lv^a, Liyan Shen^{a,*},
Yangang Wang^{a,*}

^a Department of Endocrinology, Affiliated Hospital of Medical College Qingdao University, Qingdao, China

^b Institute of Biophysics, Chinese Academy of Sciences, University of Chinese Academy of Sciences, Beijing, China

This is an example of one of over 125 journal articles reviewing this topic on the CDC website Evidence used to update the list of underlying medical conditions that increase a person's risk of severe illness from COVID-19. [CDC.gov/coronavirus/2019-ncov/need-extra-precautions/evidence-table](https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/evidence-table): Accessed 21 Jan 2021



~1.5-3 fold
increased
risk of
poor
outcomes

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.

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



INSULIN RESISTANCE

There is no need to have a degree in biochemistry in order to understand insulin resistance. Pathways are complicated, as shown by this picture of fructose metabolism in the liver, first described in 2010. We can all still gain an understanding how to improve our chances of having better metabolic health without confusion

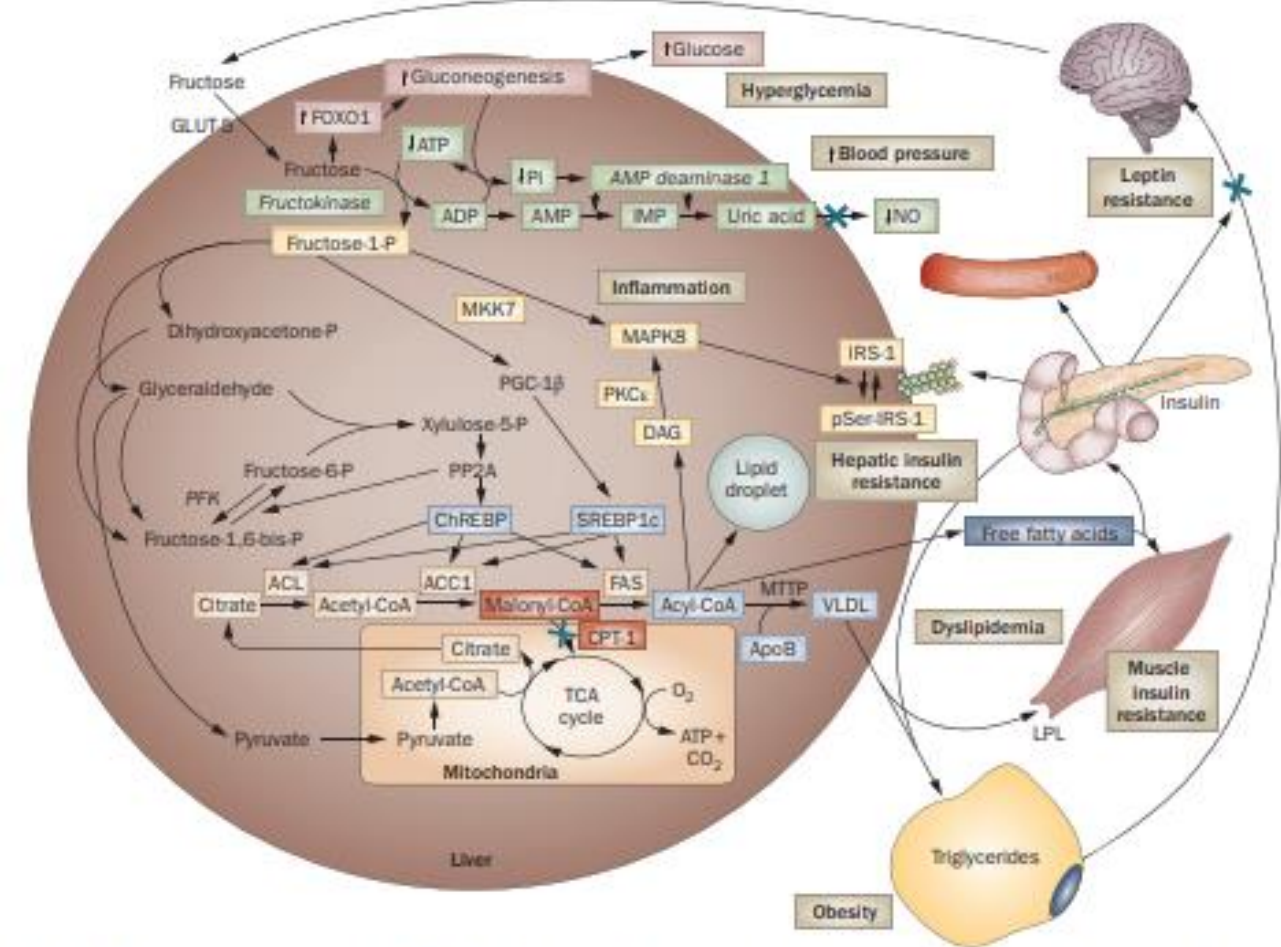
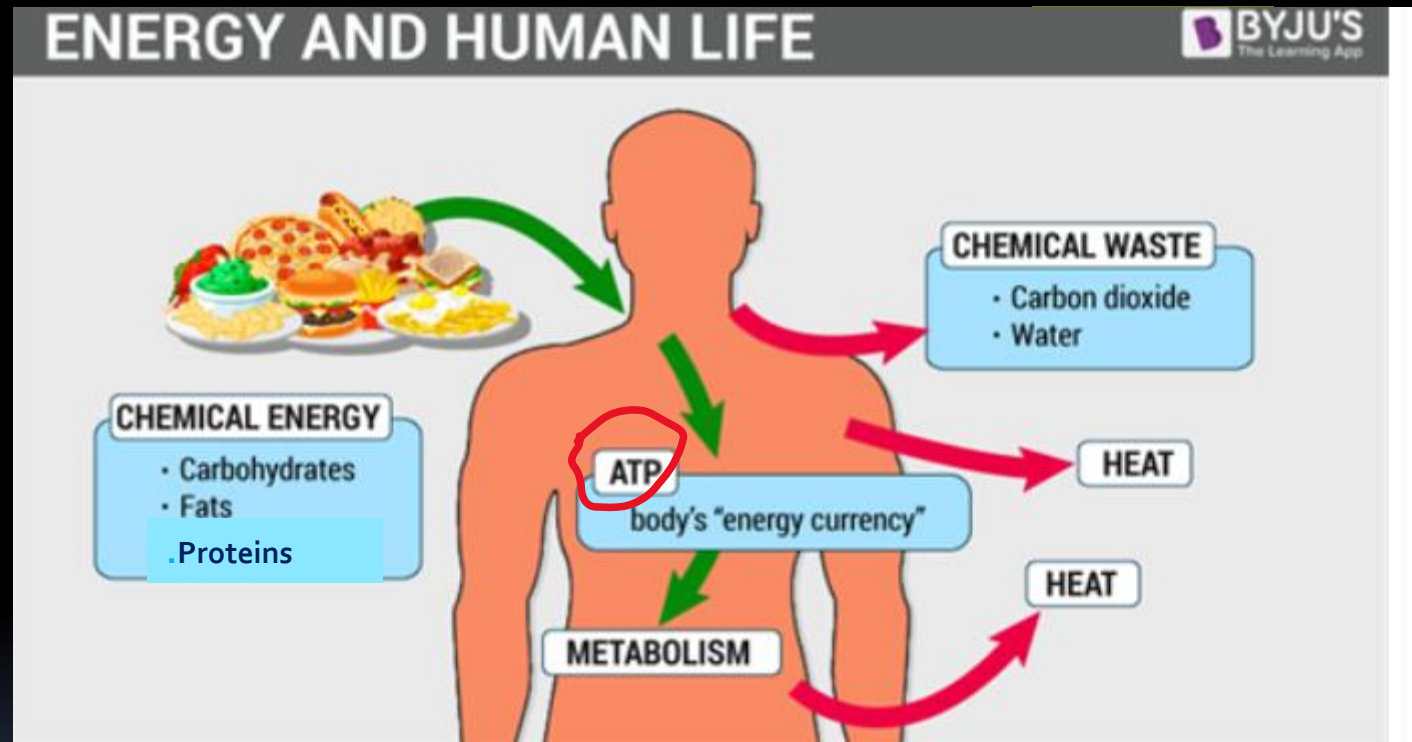


Figure 2 | Hepatic fructose metabolism. Fructose induces: substrate-dependent phosphate depletion, which increases uric acid and contributes to hypertension through inhibition of endothelial nitric oxide synthase and reduction of NO (green); excess formation of citrate, which serves as the substrate for de novo lipogenesis (orange); excess formation of malonyl-CoA, which inhibits β -oxidation (red); hepatic lipid droplet formation and steatosis; activation of MAPK8 and PKC ϵ , which contributes to serine phosphorylation of IRS-1 and hepatic insulin resistance, which in turn promotes hyperinsulinemia and influences substrate deposition into fat (yellow); export of free fatty acids, which leads to VLDL formation and muscle insulin resistance (light blue); increased synthesis of FOXO1, which promotes gluconeogenesis and hyperglycemia (pink); and central nervous system hyperinsulinemia, which antagonizes central leptin signaling and promotes continued energy intake. Abbreviations: ACL, ATP-citrate lyase; ACC1, acetyl-CoA carboxylase 1; apo B, apolipoprotein B-100; ChREBP, carbohydrate response element binding protein; CPT-1, carnitine O-palmitoyl transferase 1; FAS, fatty acid synthase; DAG, diacylglycerol; FOXO1, forkhead box protein O1; GLUT-5, solute carrier family 2, facilitated glucose transporter member 5; IRS-1, insulin receptor substrate 1; LPL, lipoprotein lipase; MAPK8, mitogen-activated protein kinase 8; MKK7, mitogen-activated protein kinase kinase 7; MTTP, microsomal triglyceride transfer protein; NO, nitric oxide; PFK, 6-phosphofructokinase; PGC-1 β , peroxisome proliferator-activated receptor γ coactivator 1 β ; Pi, inorganic phosphate; PKC ϵ , protein kinase C ϵ type; PP2A, protein phosphatase 2a; pSer-IRS-1, serine phosphorylated IRS-1; SREBP-1c, sterol regulatory element binding protein-1c; TCA, tricarboxylic acid.

Lim J S et al. The role of fructose in the pathogenesis of NAFLD and the metabolic syndrome. . *Nat. Rev. Gastroenterol. Hepatol.* 2010;7:251–264.

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

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)

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) < 1.7 mmol/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.

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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.

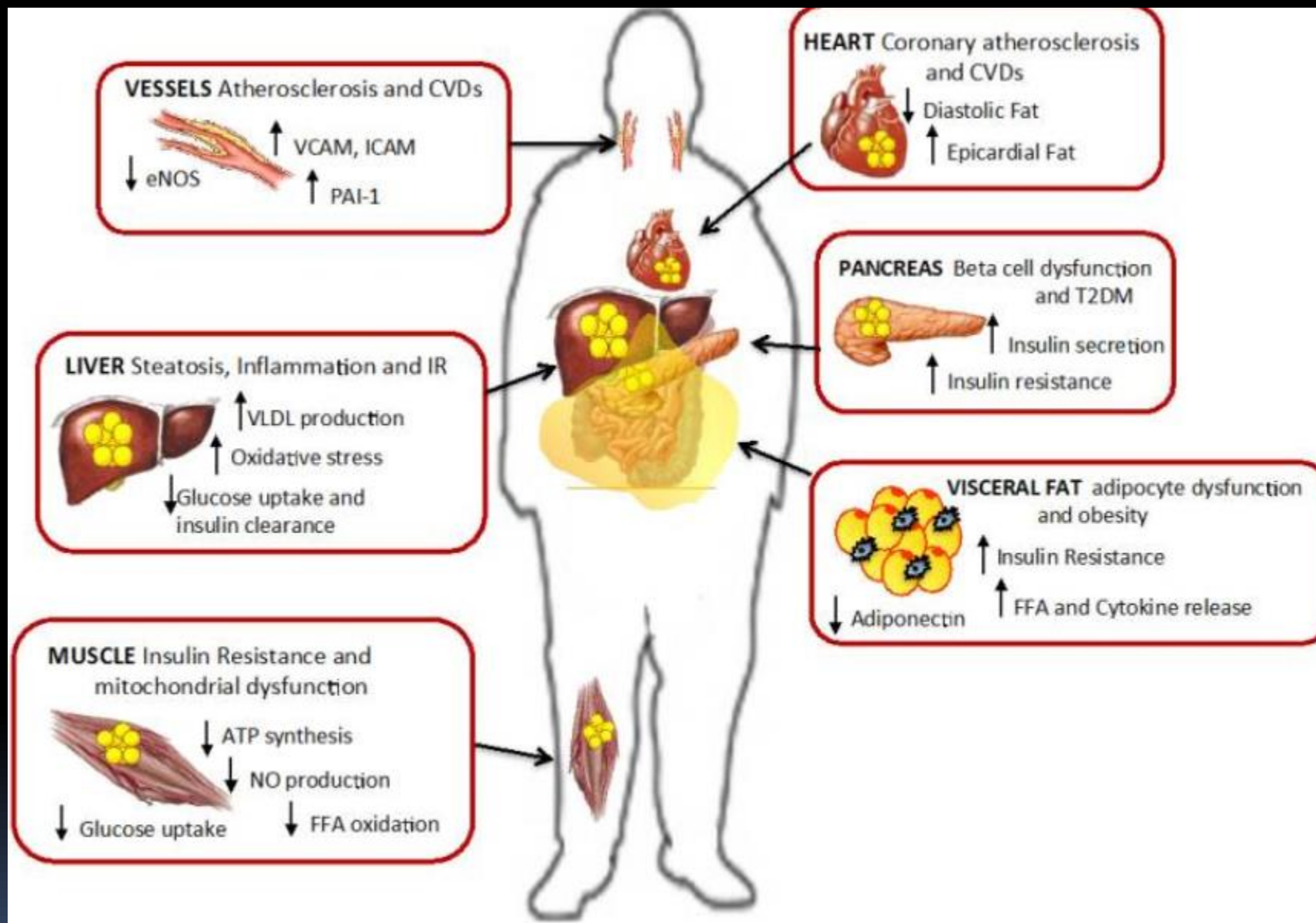


Fig. 6 Ectopic fat accumulation and effect of lipotoxicity. Fat accumulation in non-adipose tissues promotes cell dysfunction, insulin resistance and inflammation in liver, muscle, pancreas and visceral fat. Also, in vessels and heart lipotoxicity leads to increased risk for cardiovascular diseases and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

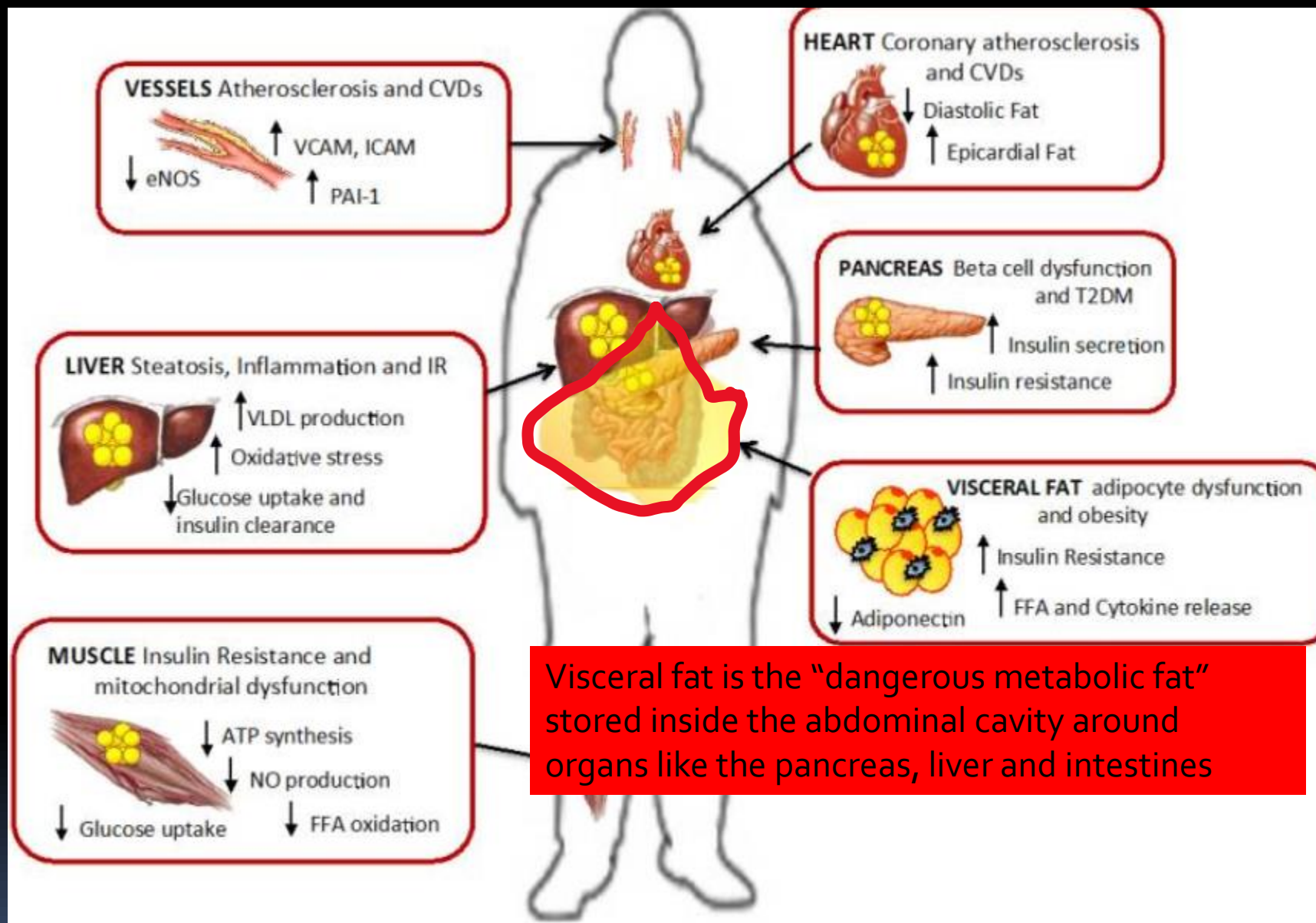


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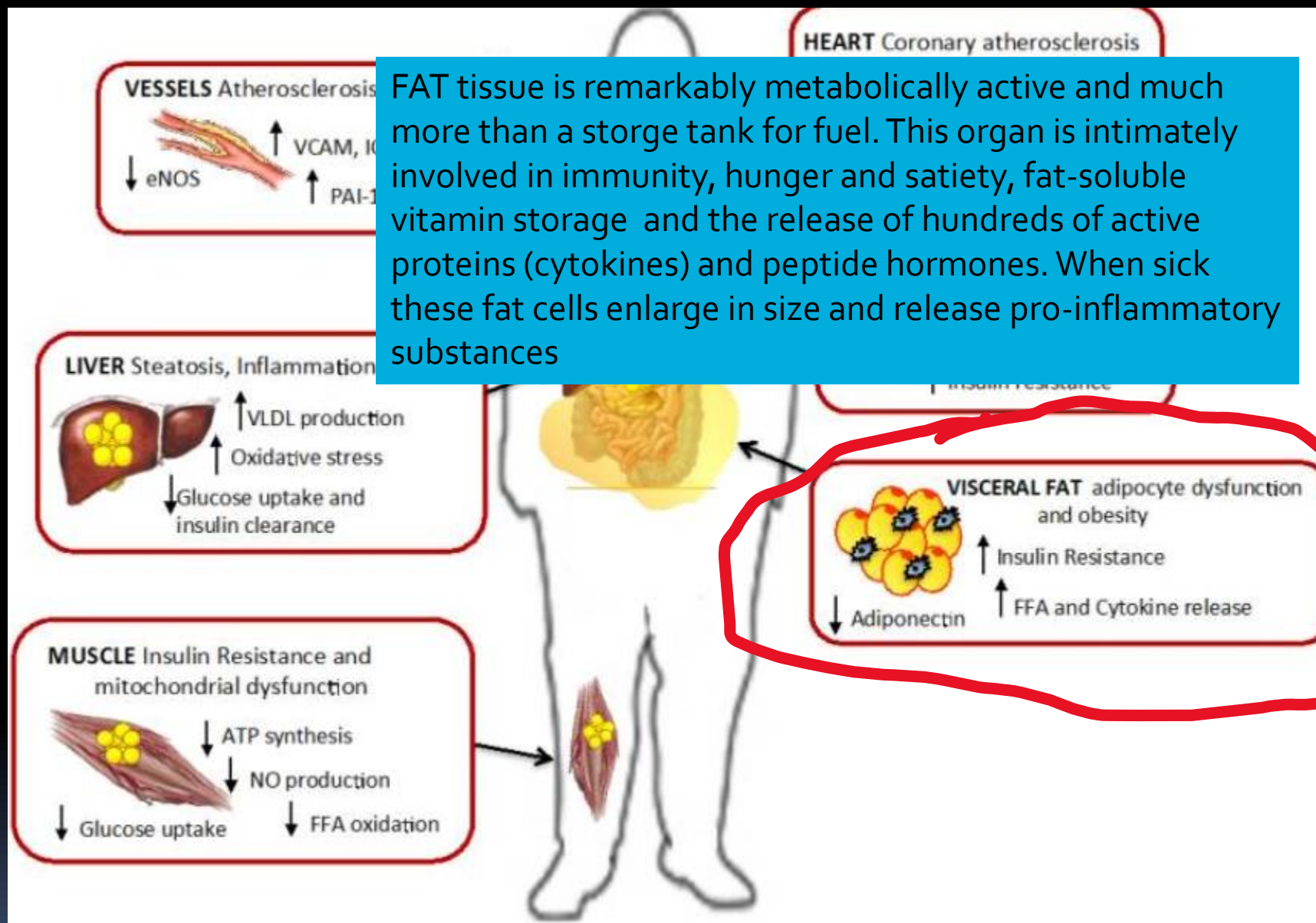


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Visceral fat in the liver produces “fatty liver” (Non-alcoholic fatty liver disease; NAFLD). Your liver starts producing more fat and exports it to other areas of the body in VLDLs which convert to SMALL DENSE LDLs; strongly associated with cardiovascular 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.

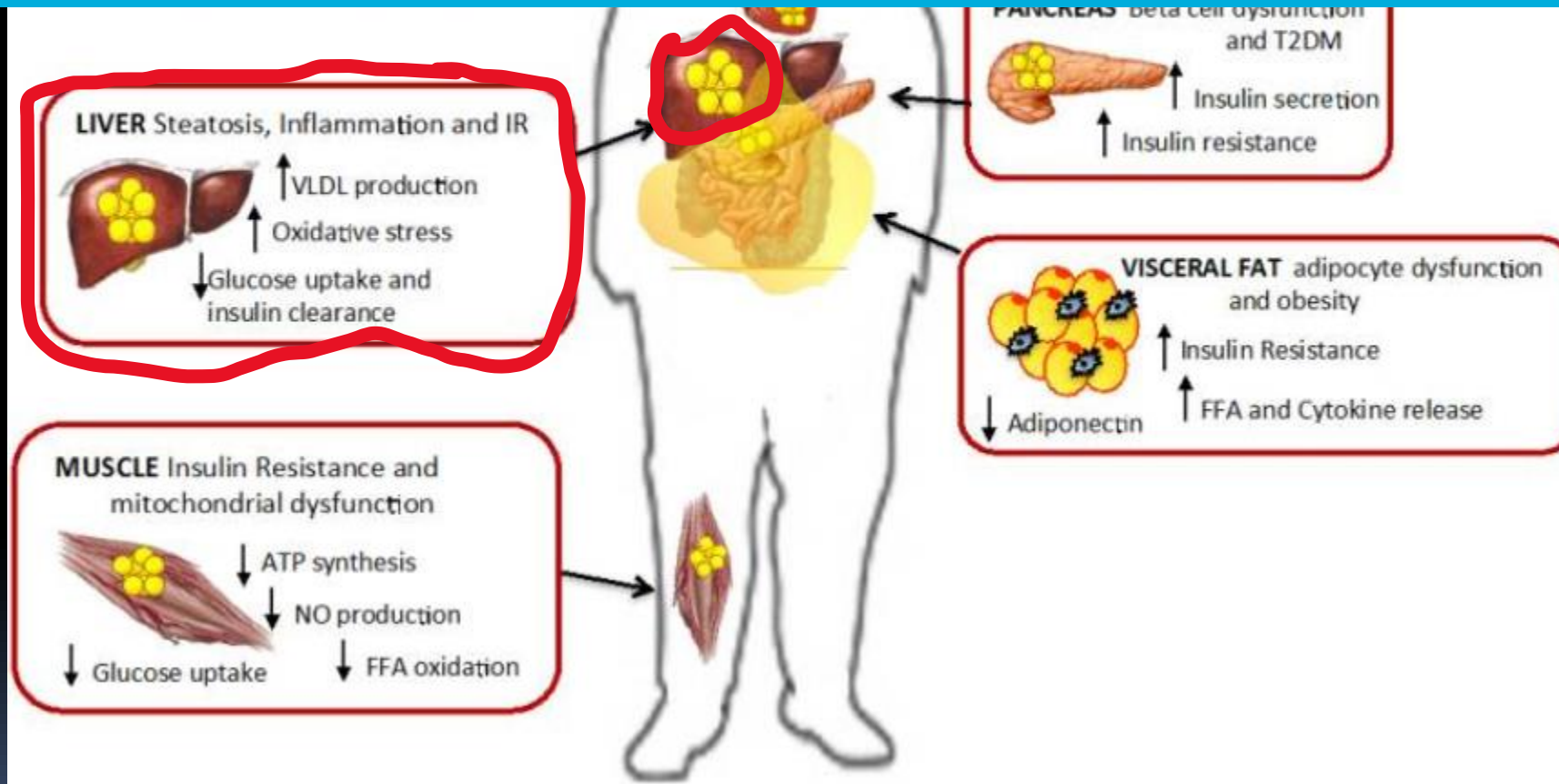


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The pancreas is “stressed out” trying to pump out more insulin to control toxic high blood sugar levels. The higher the insulin rises the greater the insulin resistance becomes in tissues like liver, adipose tissue (fat cells), and muscle. Eventually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

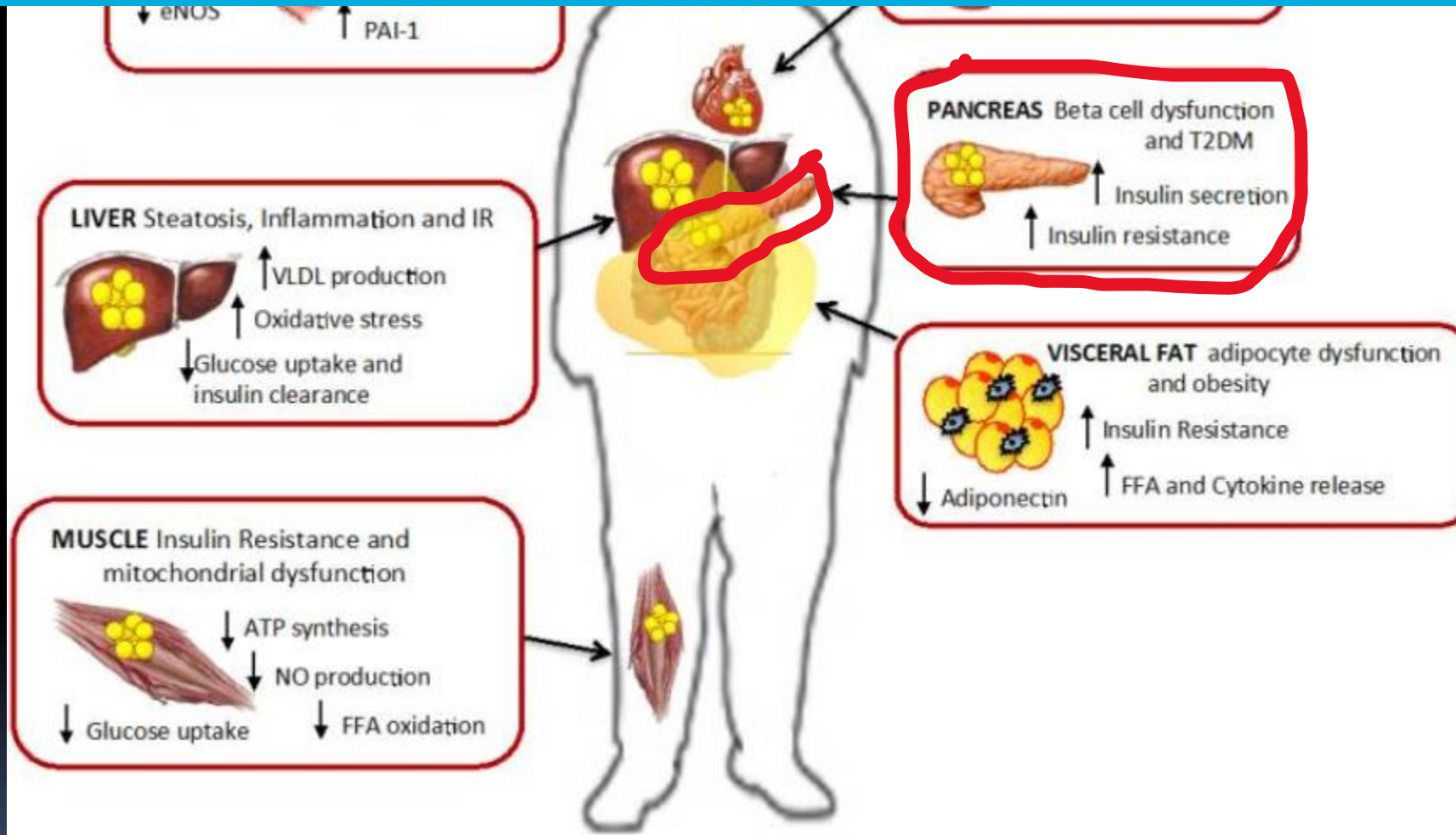
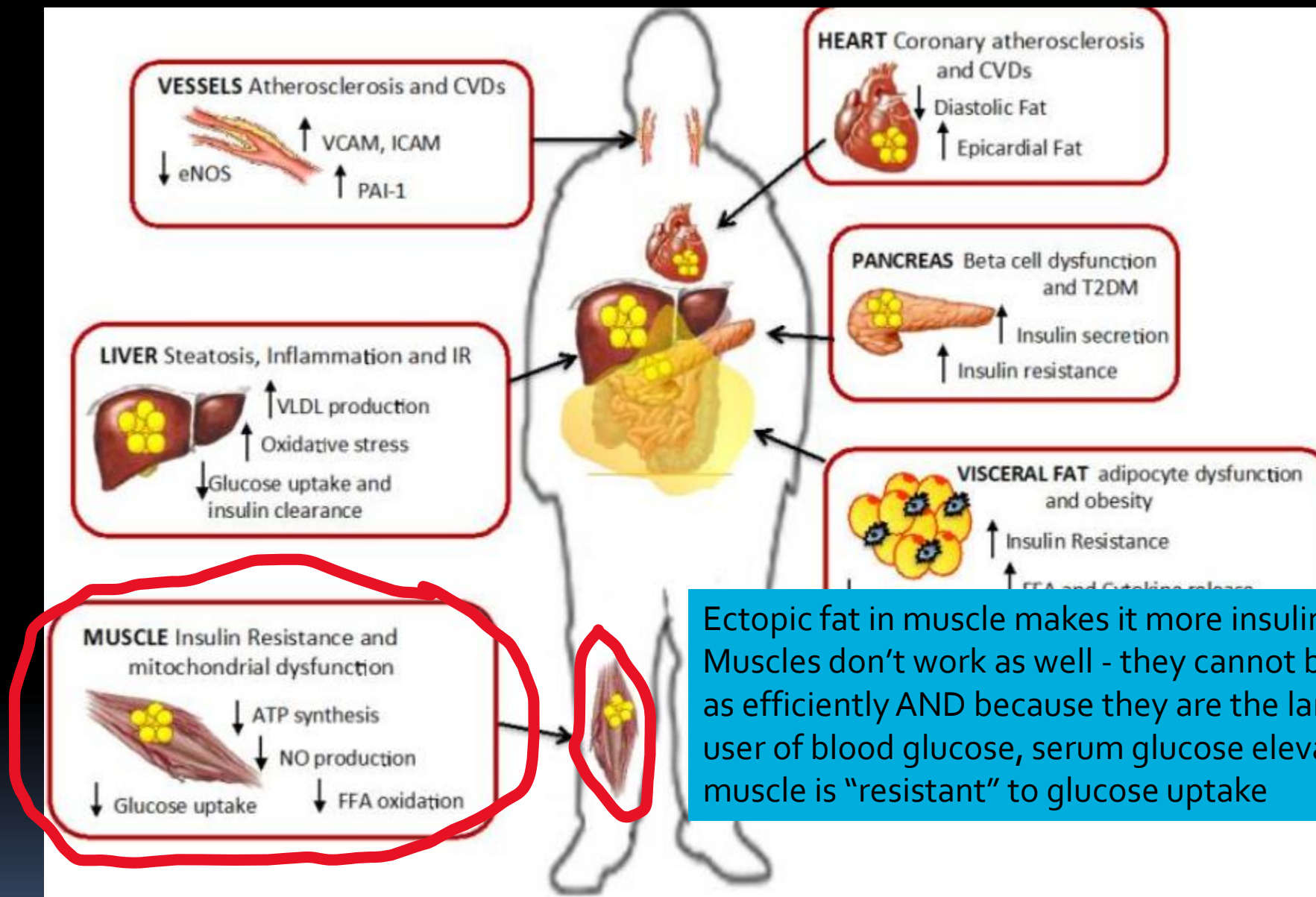
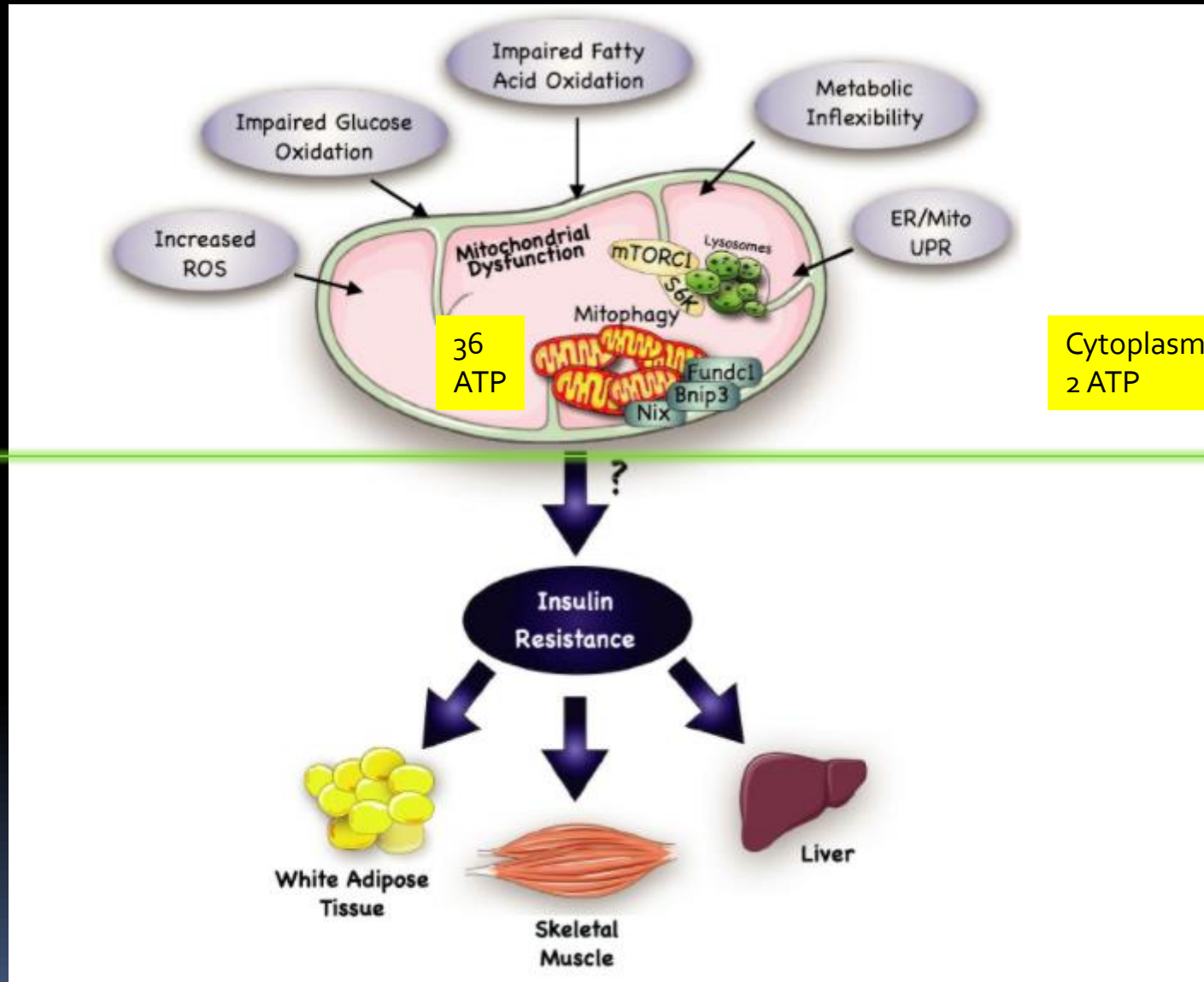


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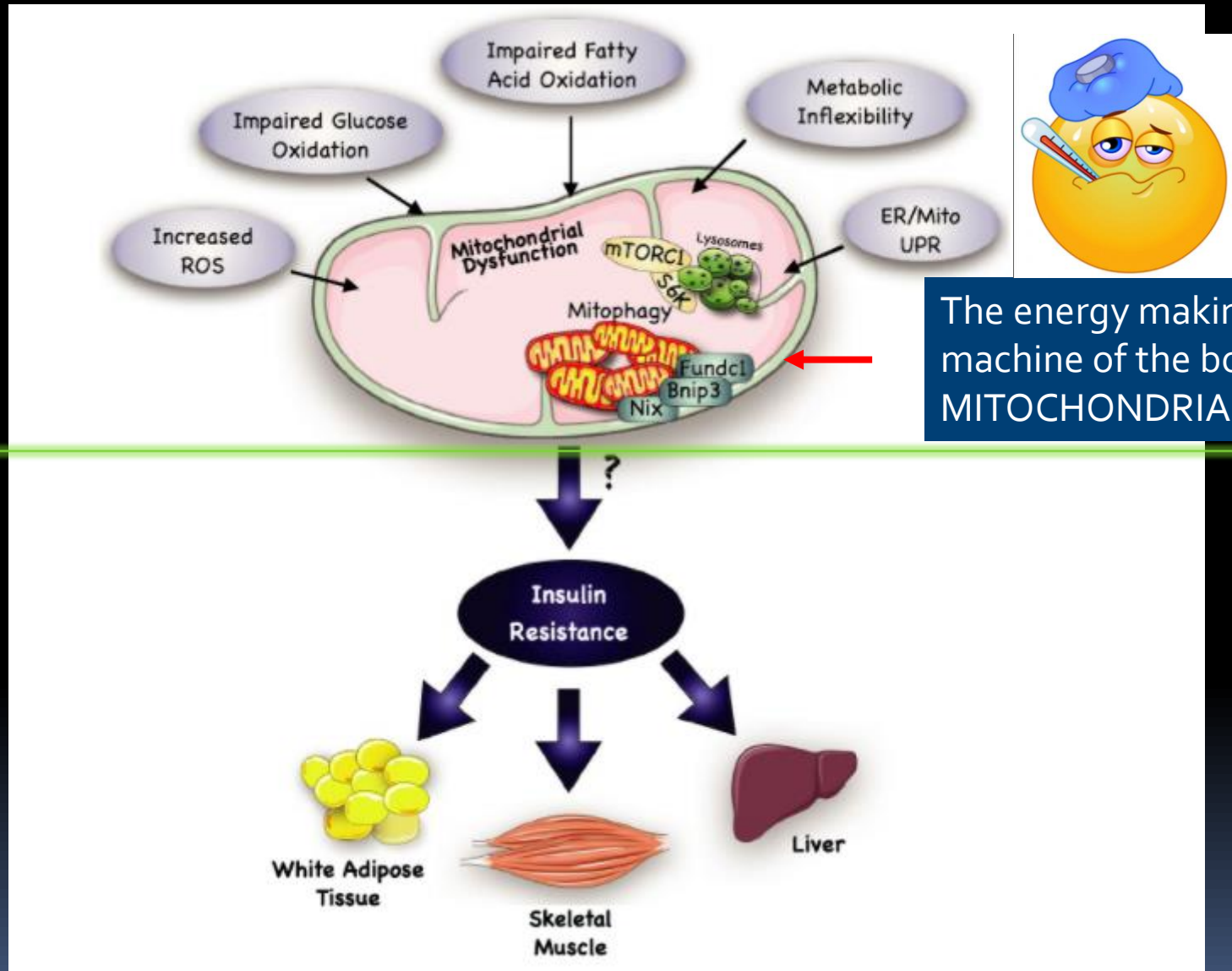


Ectopic fat in muscle makes it more insulin resistant. Muscles don't work as well - they cannot burn fat for fuel as efficiently AND because they are the largest SINK, or user of blood glucose, serum glucose elevates since the muscle is "resistant" to glucose uptake

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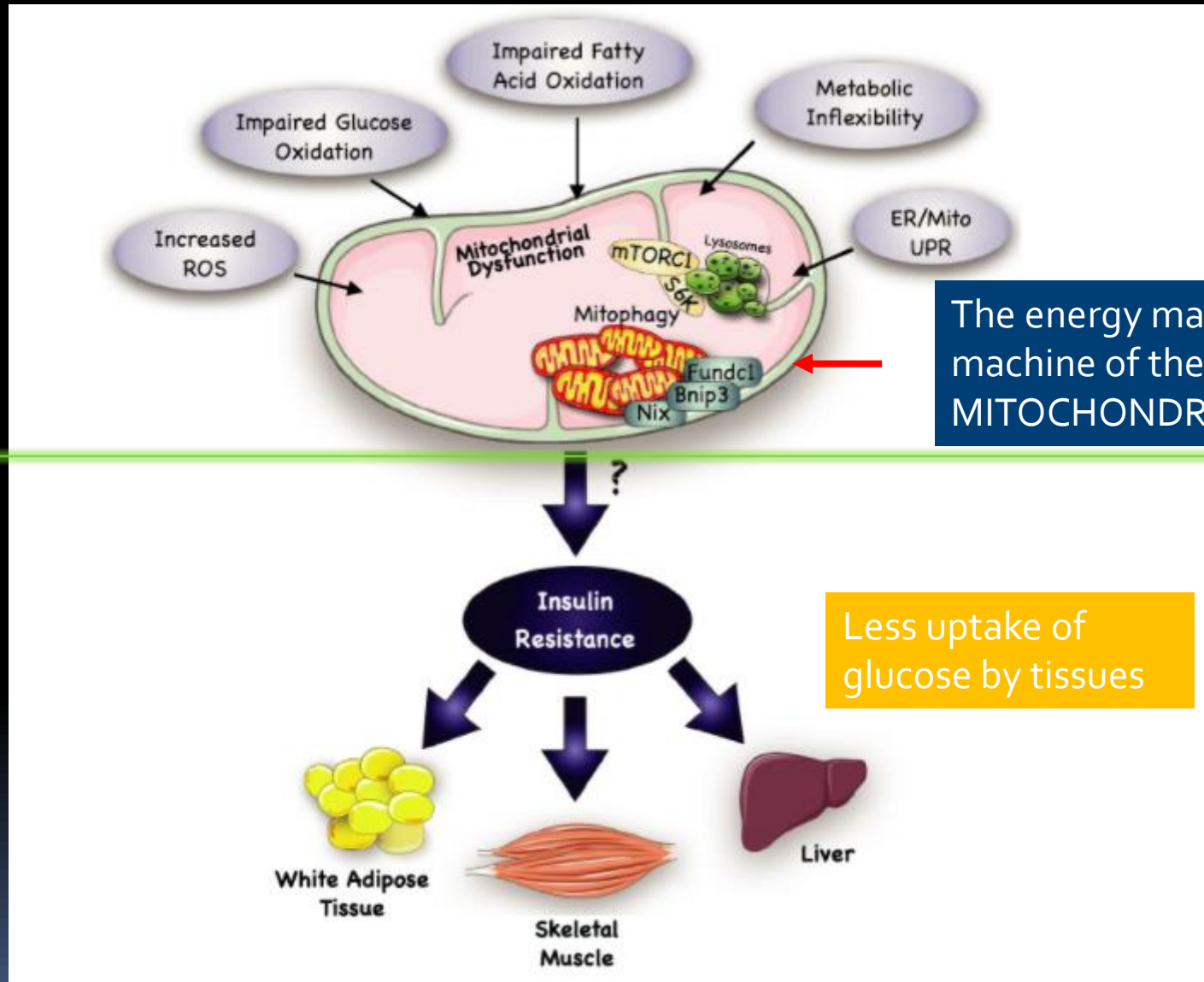


Cell
Body



The energy making machine of the body
MITOCHONDRIA

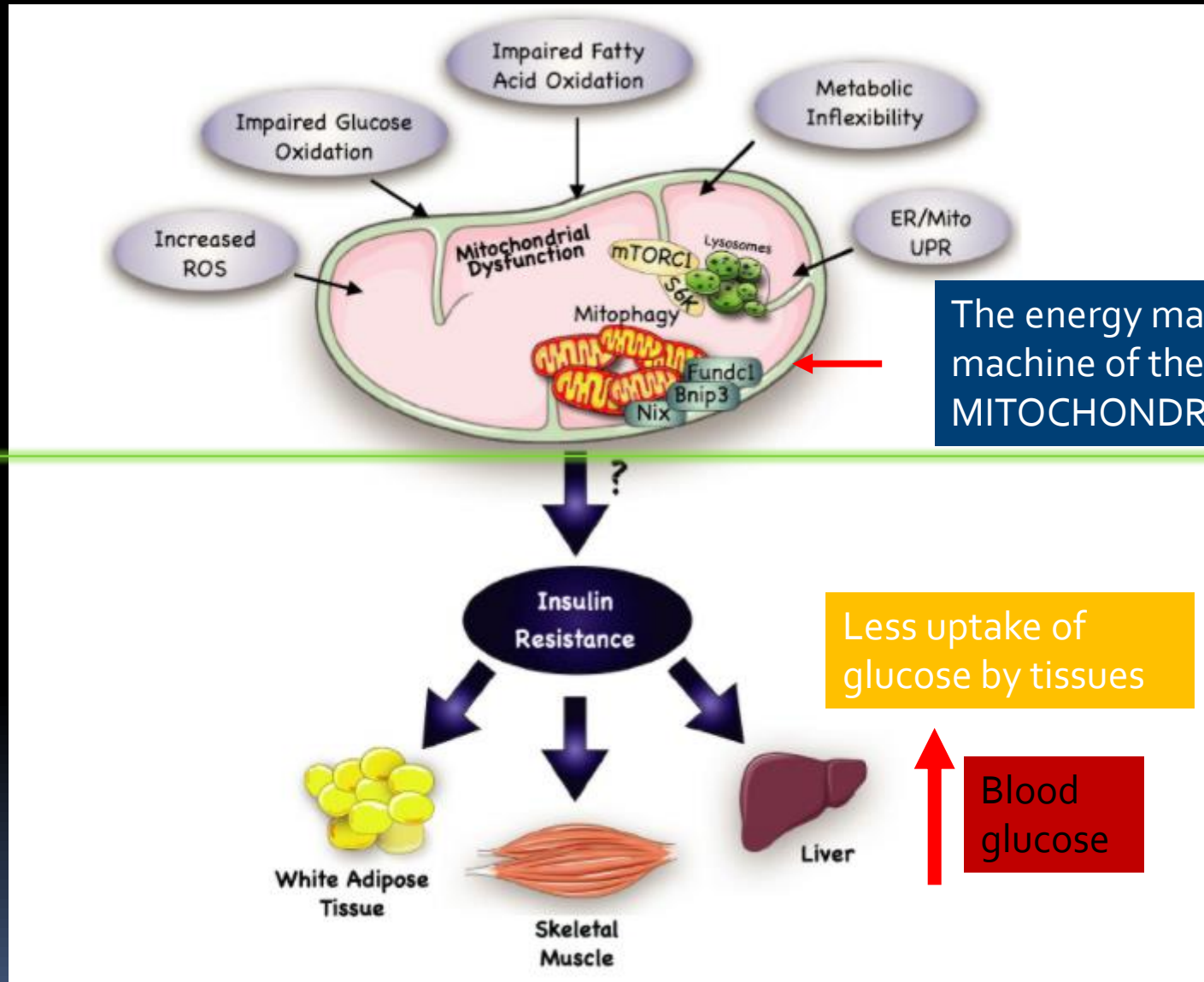
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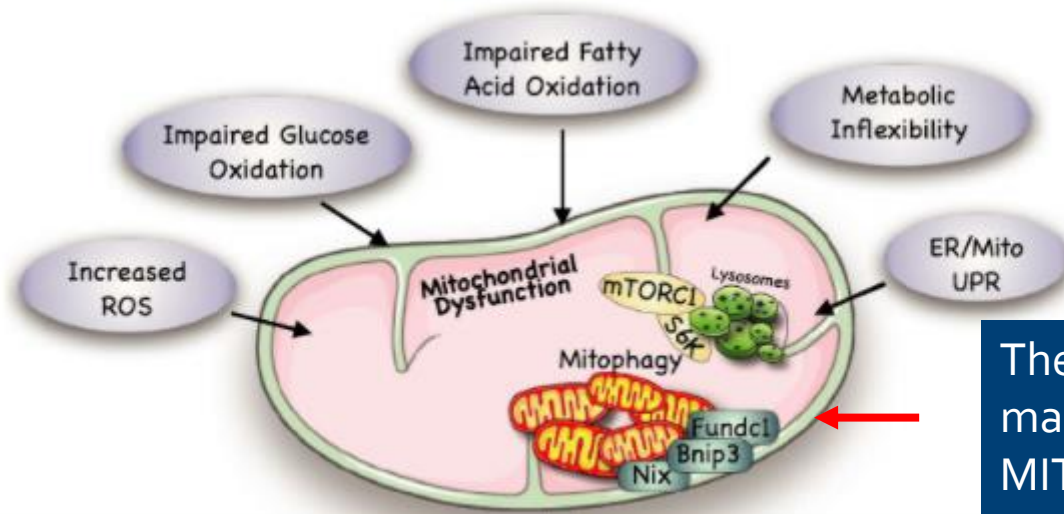
Cell
Body

The energy making
machine of the body
MITOCHONDRIA

Less uptake of
glucose by tissues



Glucose
receptor
impaired



The energy making
machine of the body
MITOCHONDRIA

Cell
Body



**Insulin
Resistance**

Less uptake of
glucose by tissues



White Adipose
Tissue



Skeletal
Muscle

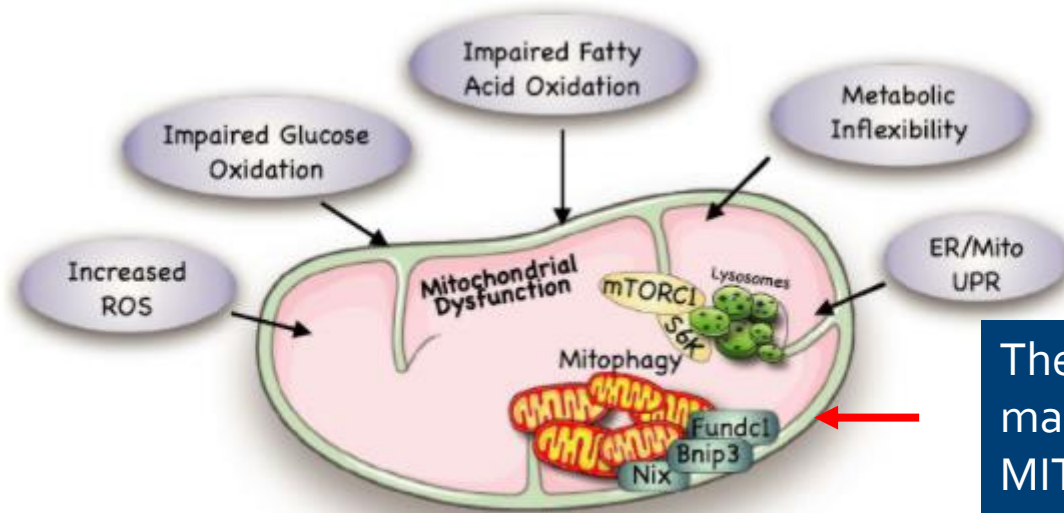


Liver



Blood
glucose

Glucose
receptor
impaired



The energy making
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MITOCHONDRIA

Cell
Body

Insulin



White Adipose
Tissue



Skeletal
Muscle



Liver

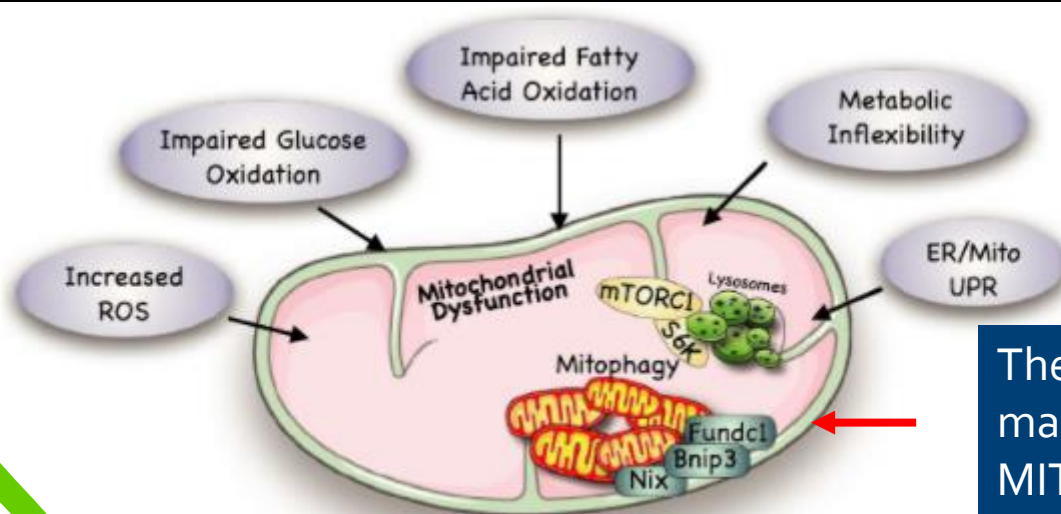
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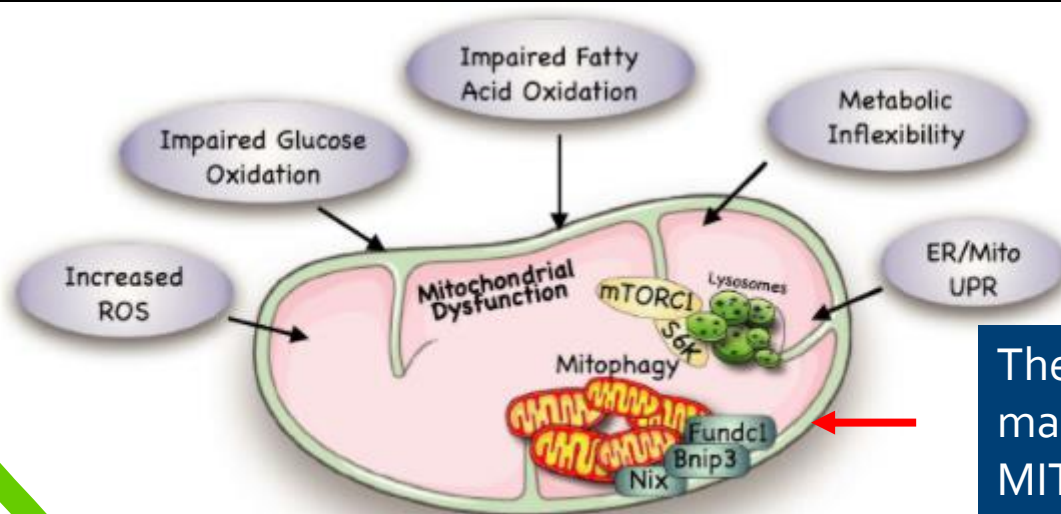
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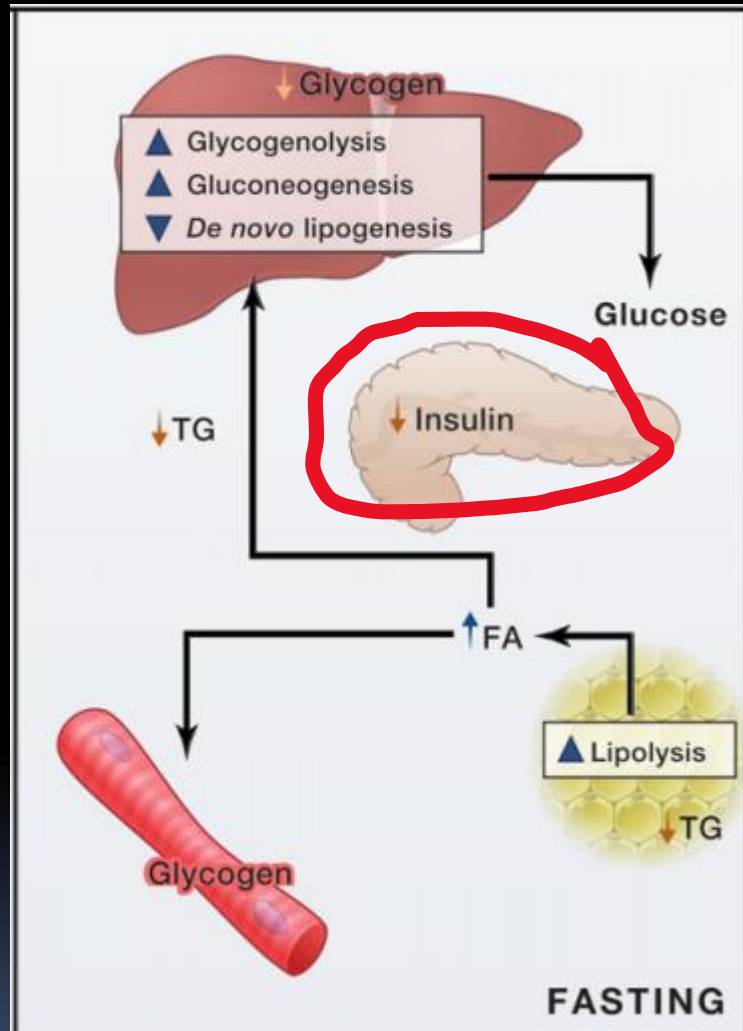
Less uptake of
glucose by tissues

Blood
glucose

White Adipose
Tissue

Skeletal
Muscle

Liver



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

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

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.

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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Association does not = Causation

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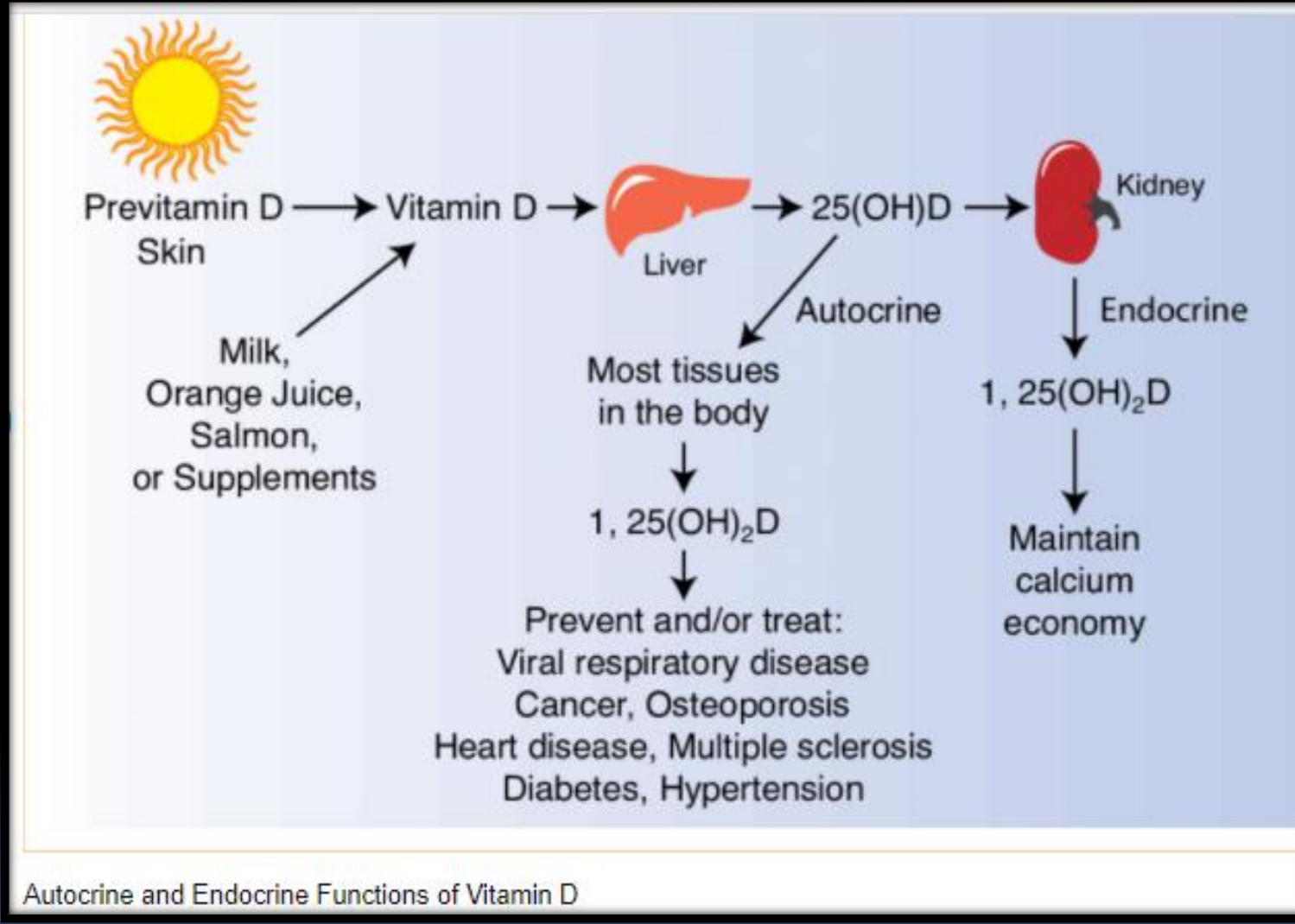
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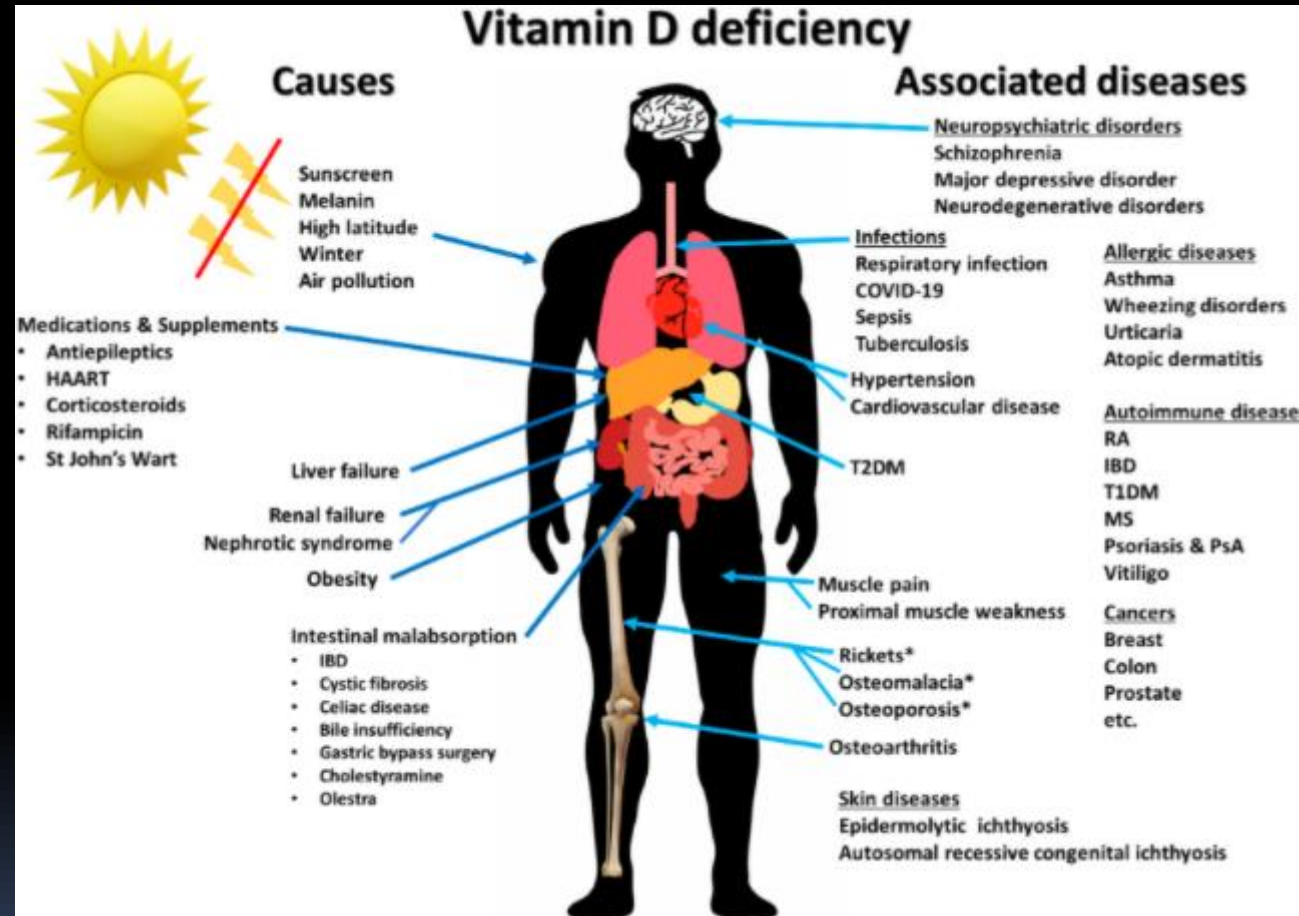
If you have enough observational studies, showing association, and the results are compelling and scientifically reasonable then we can infer CAUSATION. As an example there was a 20+ fold increase in lung cancer in smokers as compared with non-smokers. Because it was unethical to do an interventional 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.



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

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.

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

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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)
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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.

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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)

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.

¹Castillo M E et al. Effect of calcifediol treatment and best available therapy on intensive care admission and mortality among patients hospitalized for COVID-19: A pilot randomized clinical study. *The Journal of Steroid Biochemistry and Molecular Biology*. 2020 Oct;203:105751

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



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

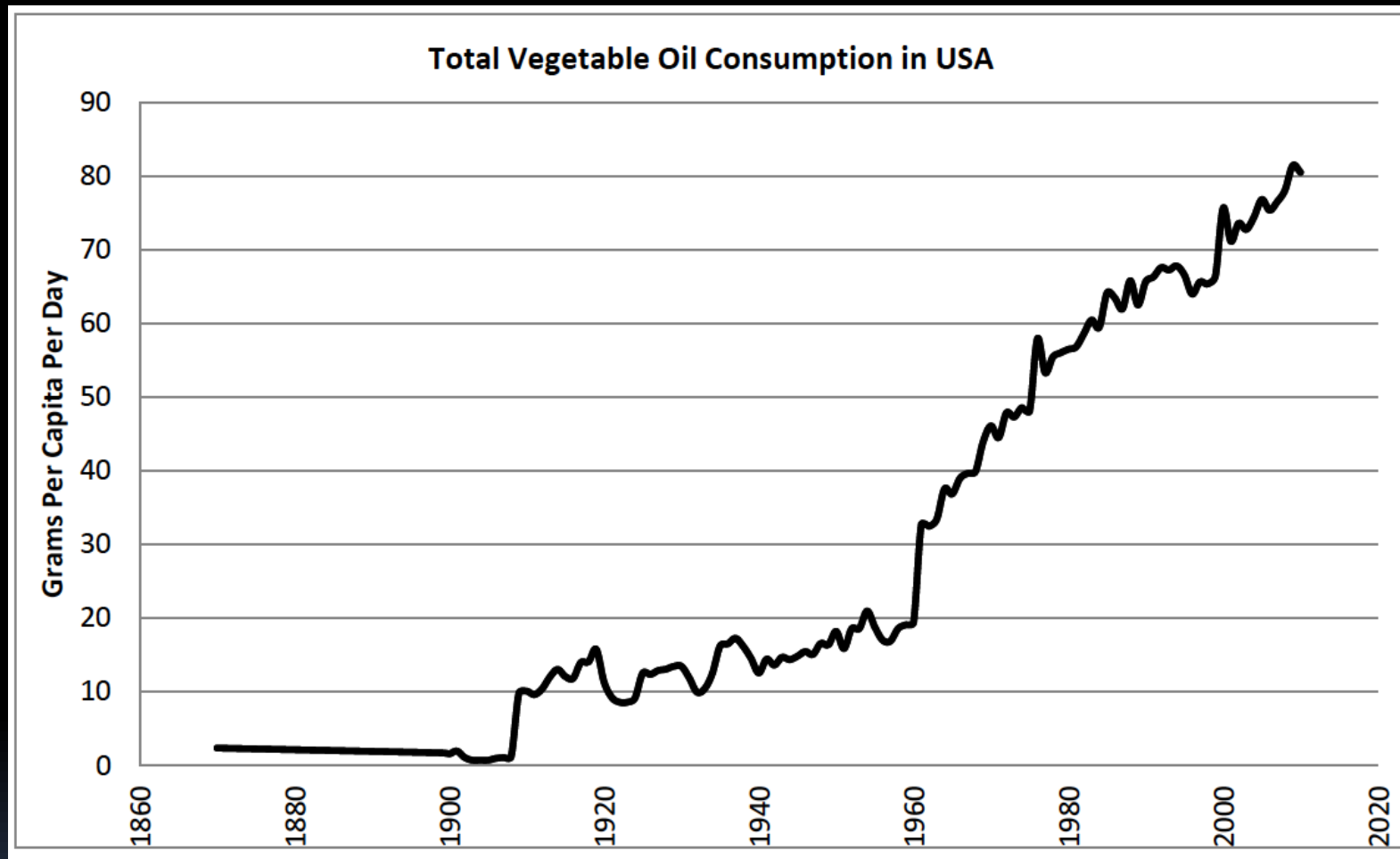
1. White Flour - 1880



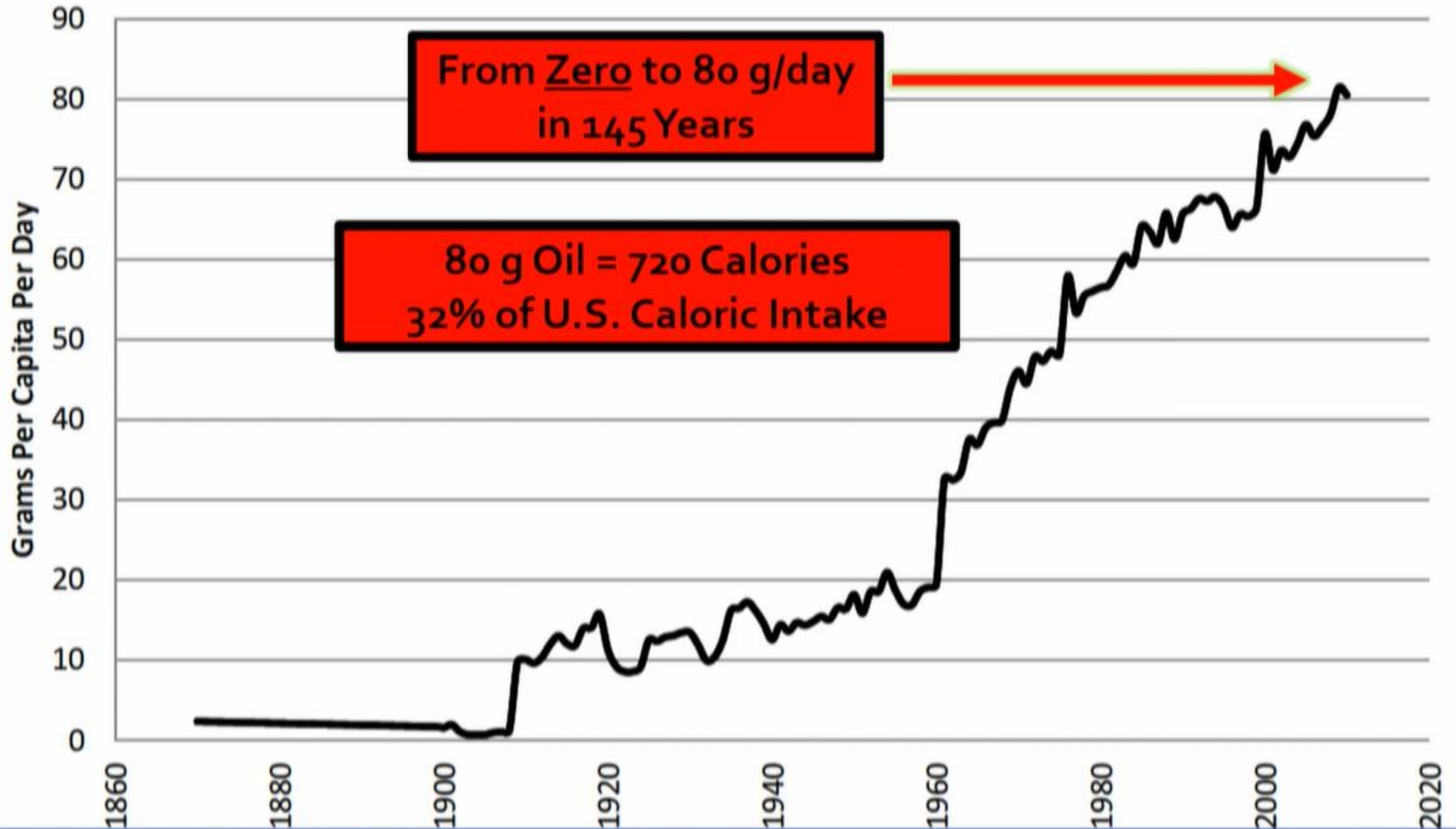
2. Vegetable Oils (PUFAs)



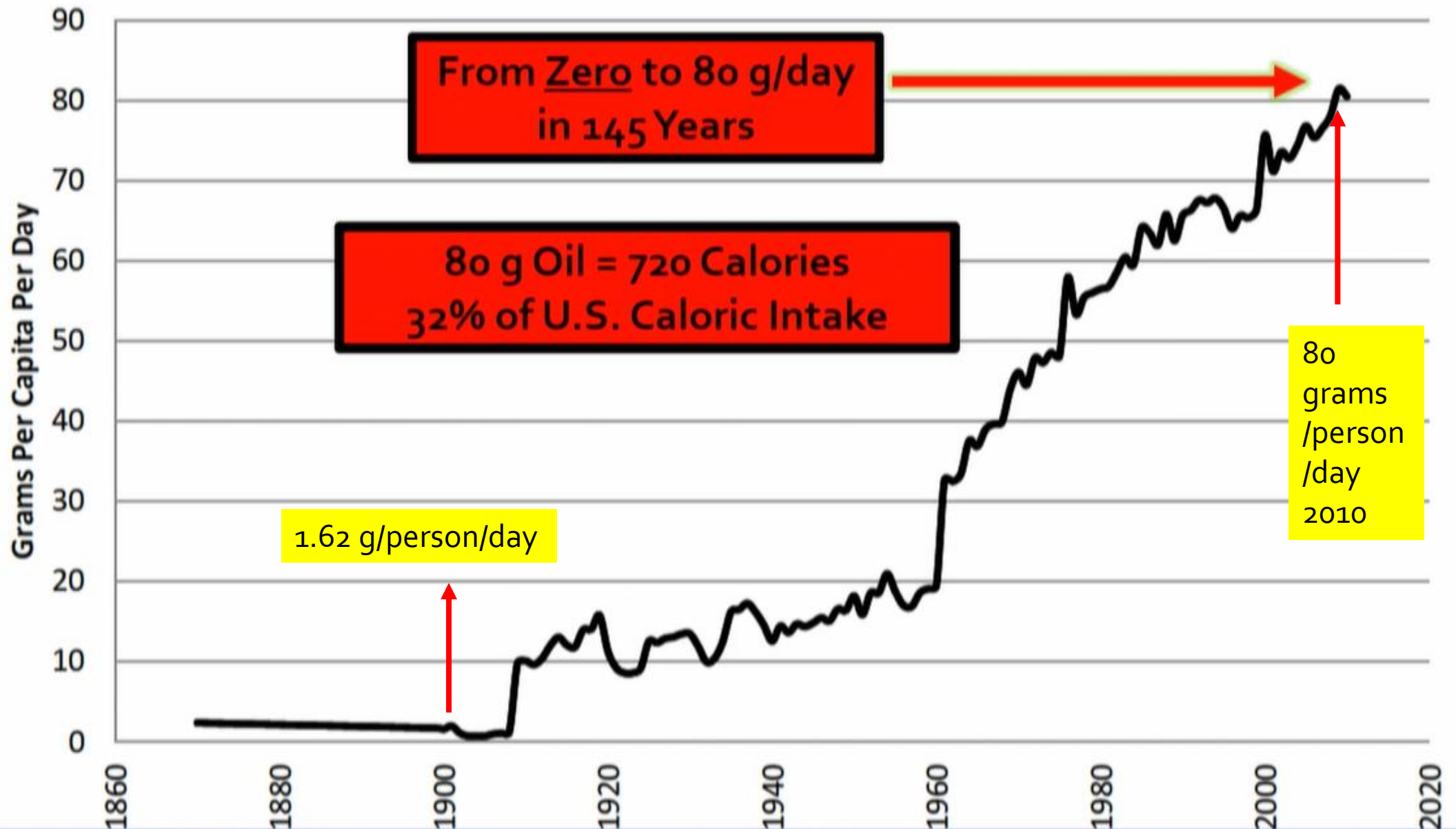
Soybean Oil
Corn Oil (Maize Germ Oil)
Cottonseed Oil
Rape/Rapeseed & Canola Oil
Sunflower Oil
Safflower Oil
Rice Bran Oil
Mustard Oil



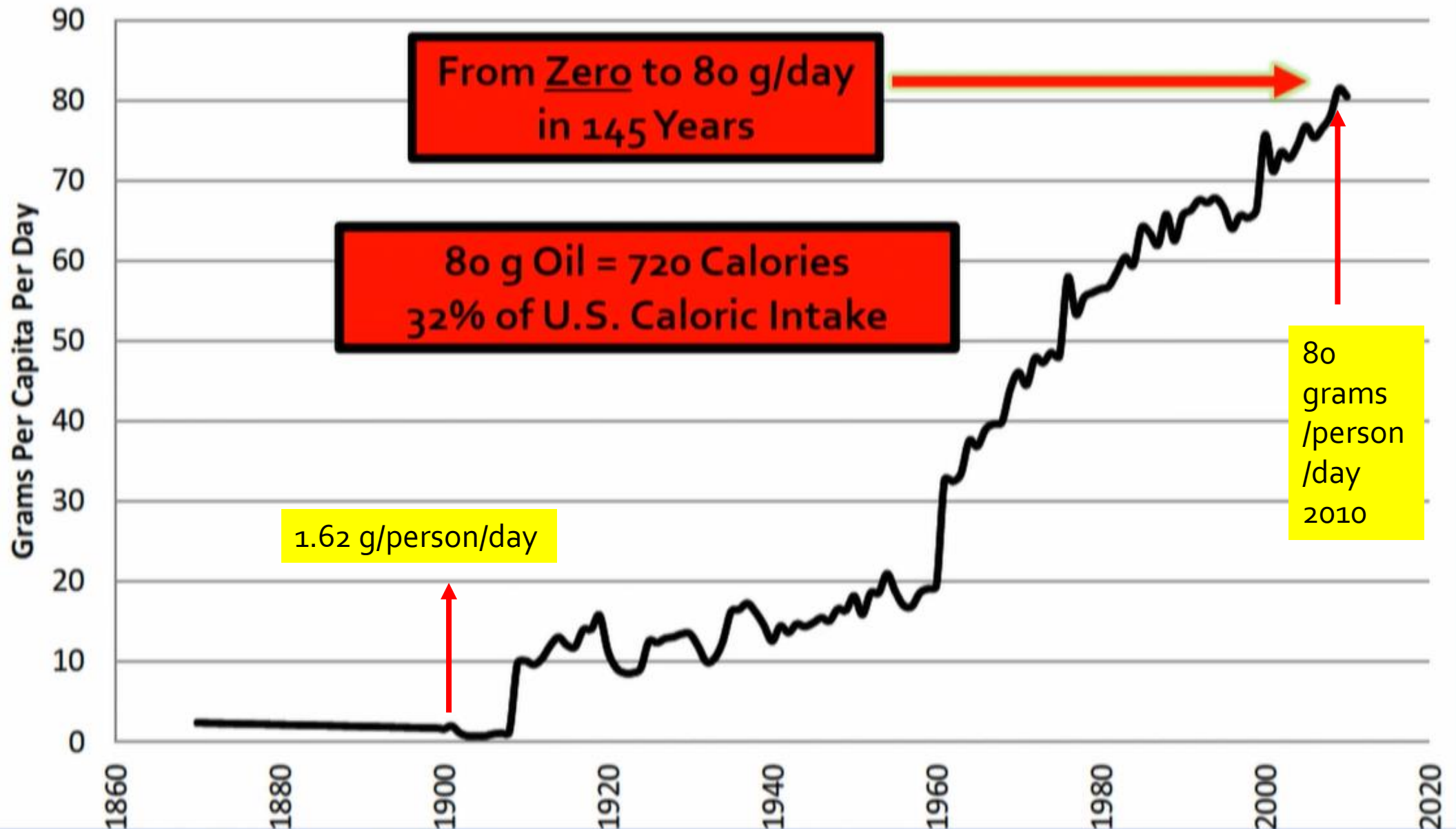
Total Vegetable Oil Consumption – USA



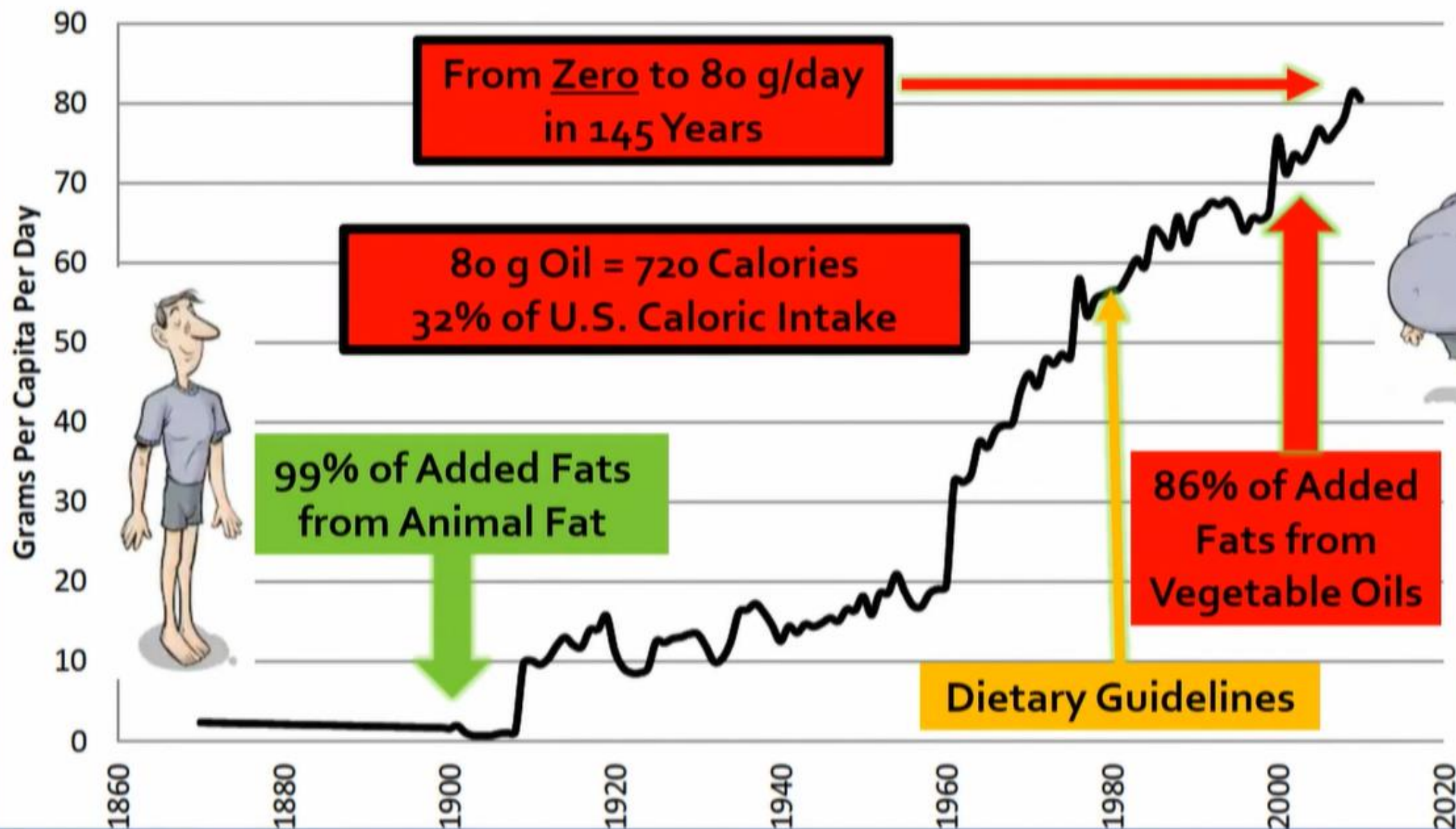
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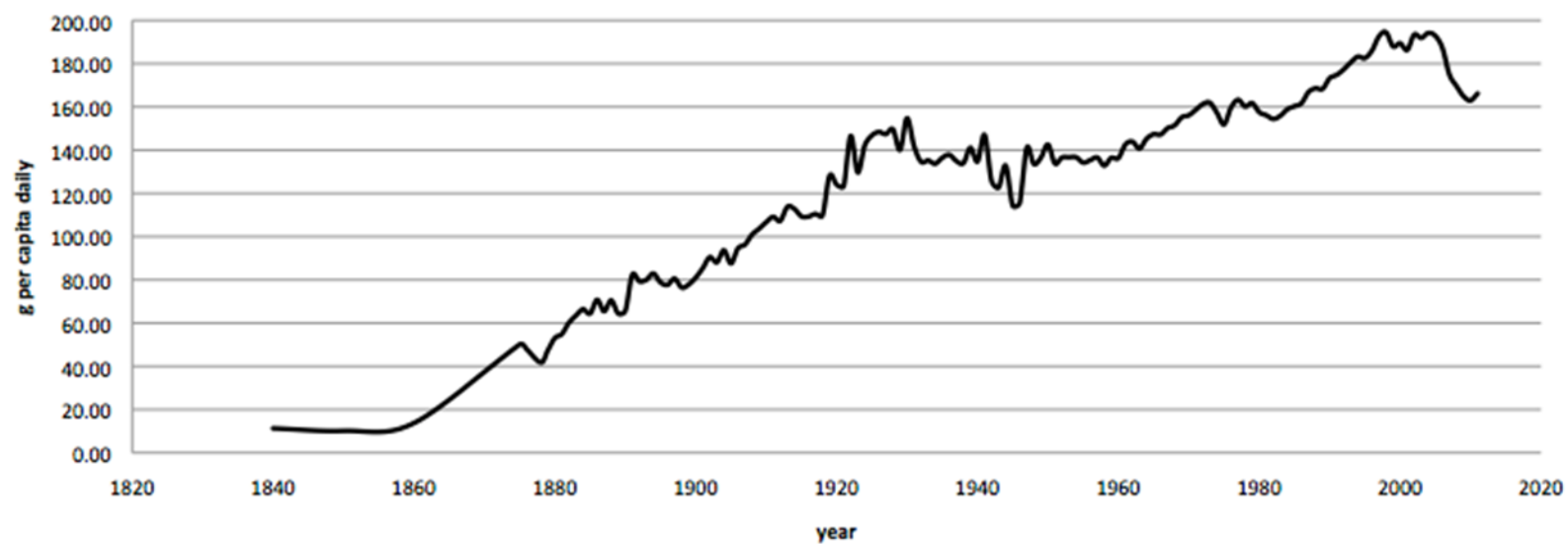


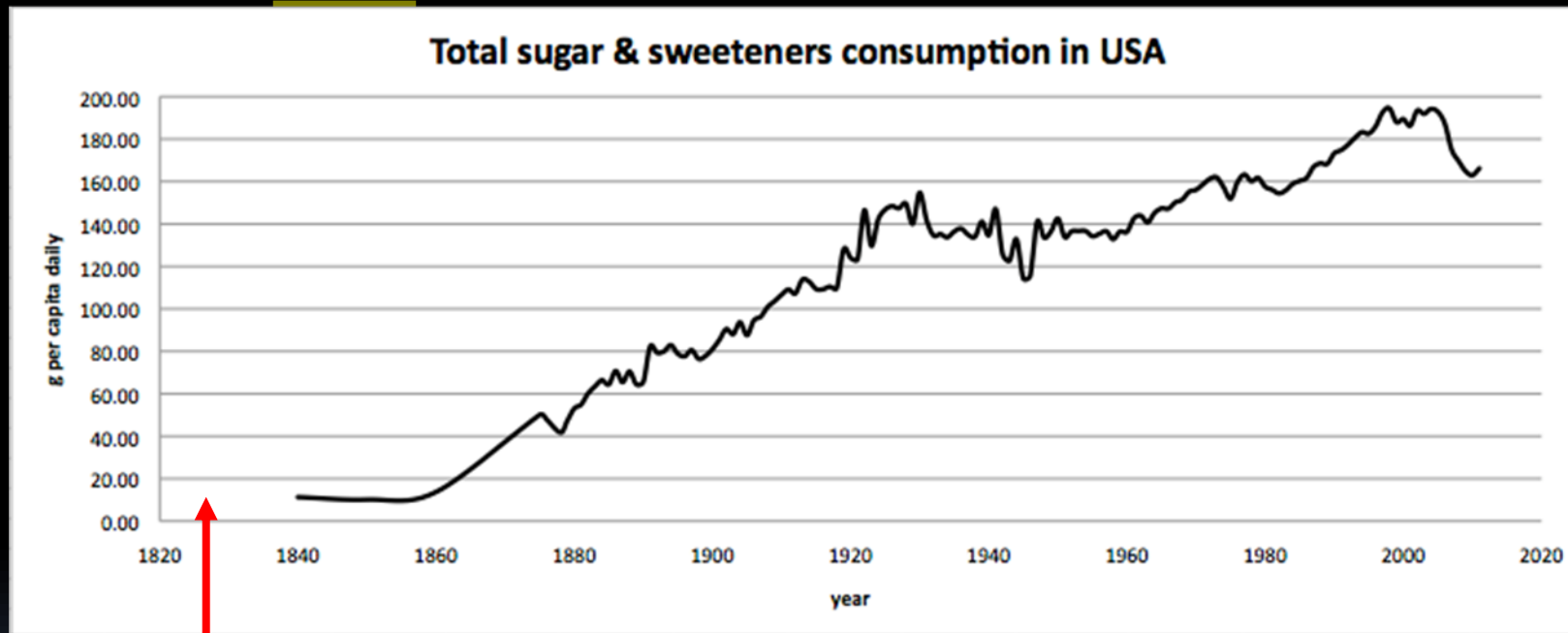
3. Trans Fats – 1911



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

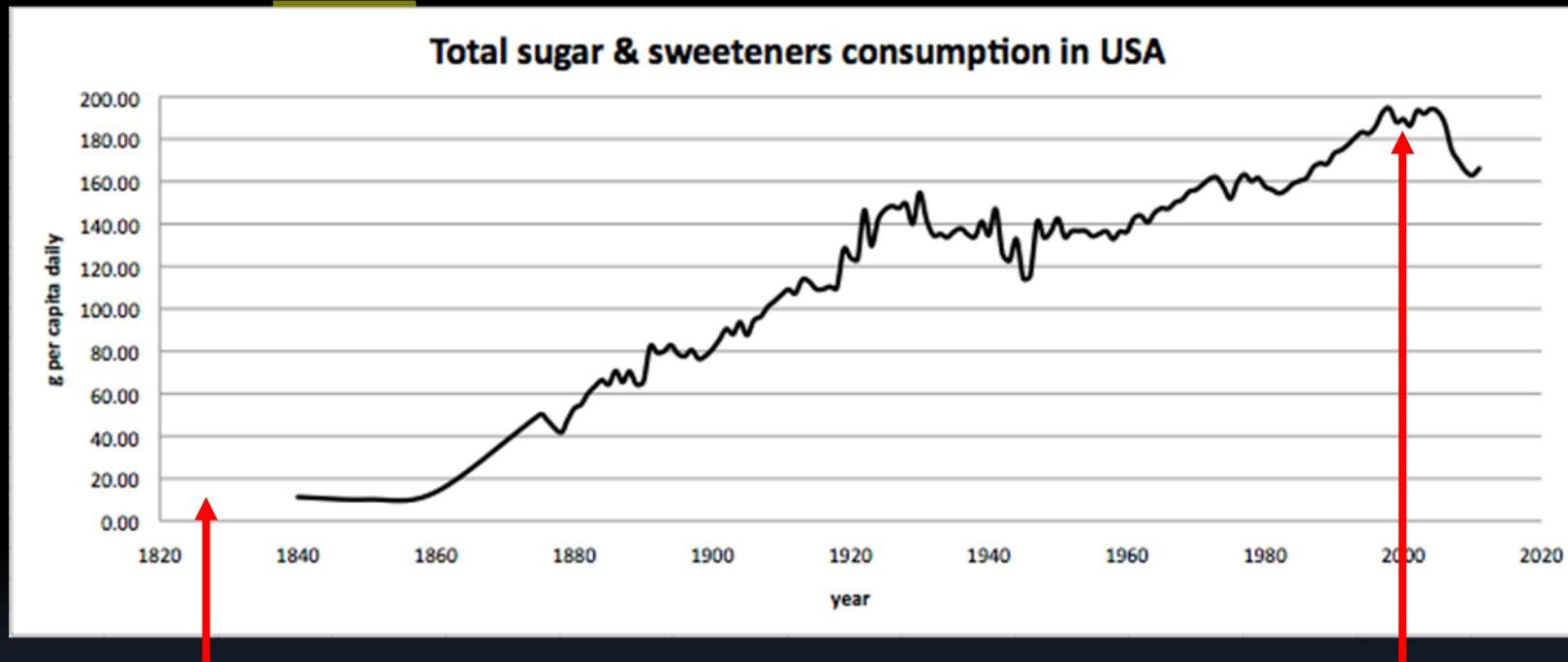
Total sugar & sweeteners consumption in USA





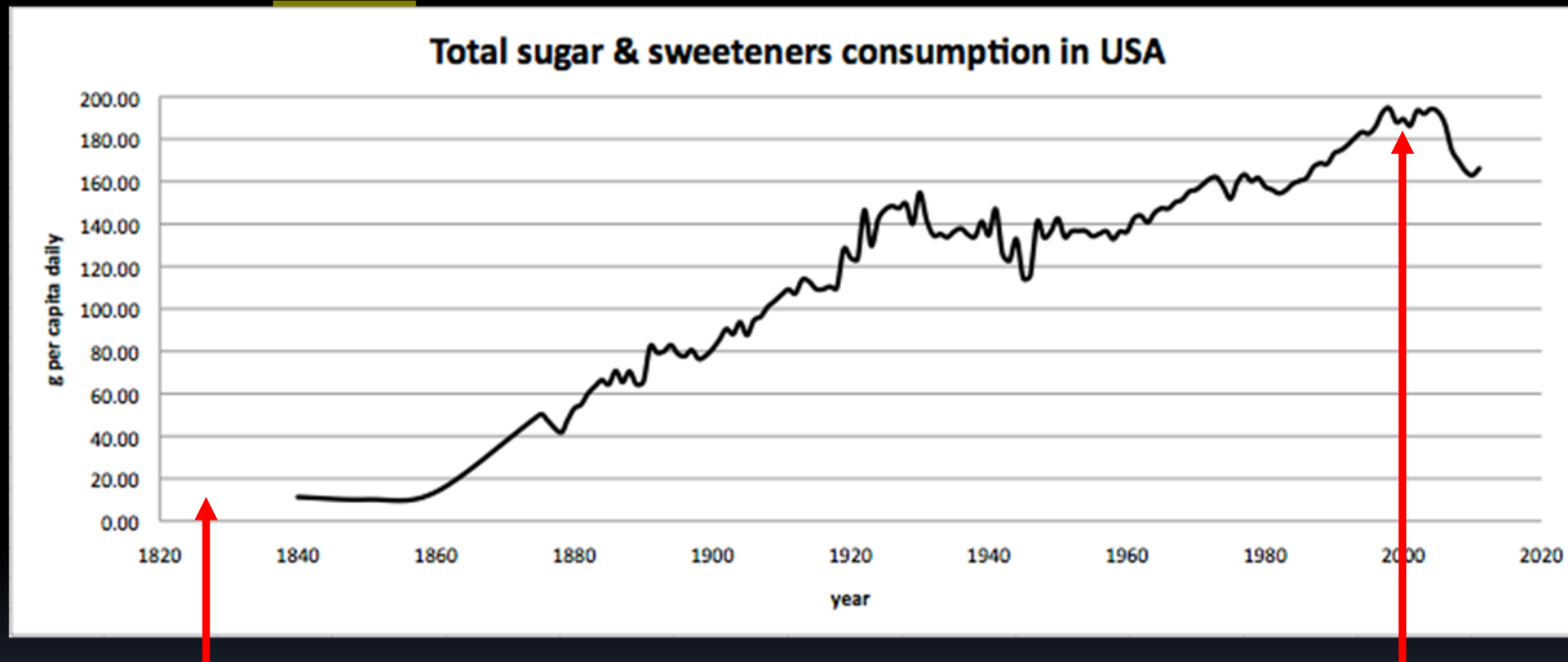
1822

1.79 tsp/person/day



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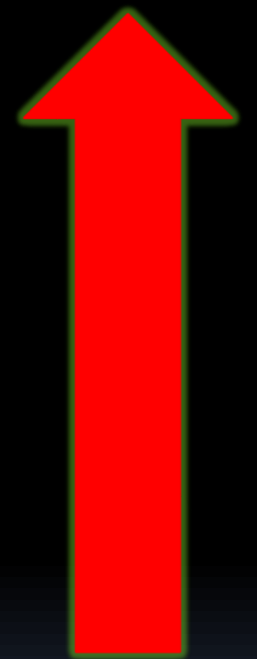
1999
32.2 tsp/person/day



1822
1.79 tsp/person/day

1999
32.2 tsp/person/day

18-fold
increase



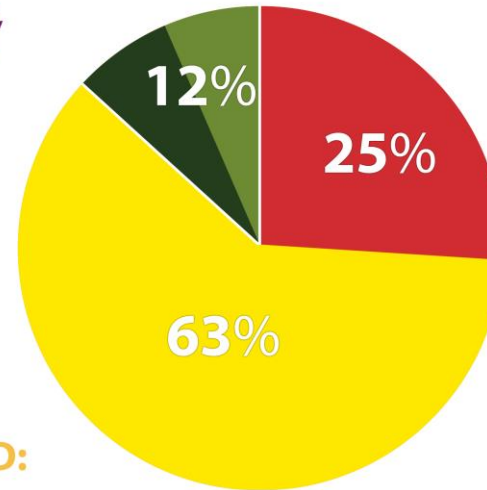
U.S. FOOD CONSUMPTION AS A PERCENT OF CALORIES - 2009

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, Stojanoska M.. Medical Hypotheses. 109 (2017) 184-198.
Source: USDA Economic Research Service, 2009; www.ers.usda.gov

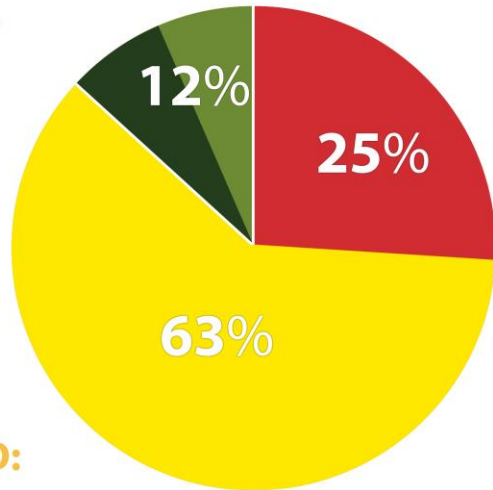
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Alcohol consumption¹

Nanos survey. Boredom and Stress Drives Increased Alcohol Consumption during COVID-19: NANOS Poll Summary Report. 2020. May.;1645:1-70: Accessed 2 Feb 2021

Barr P S et al. Impact of Alcohol Abuse on the Adaptive Immune System. *Alcohol/2 Research: Current Reviews*. 2014.;37(2):185-197

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



INSULIN RESISTANCE

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



Any glucose in the blood > 1 teaspoon (tsn.) ~4 grams , is toxic (Dr. Gary Fettke)

INSULIN RESISTANCE

“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.

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



Vegetable Oil Refinery

**Toxic
Waste!!!!**



Grass-fed Cattle

**Divinely
Healthy**

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

No Seed Oils!



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.

Thank you

