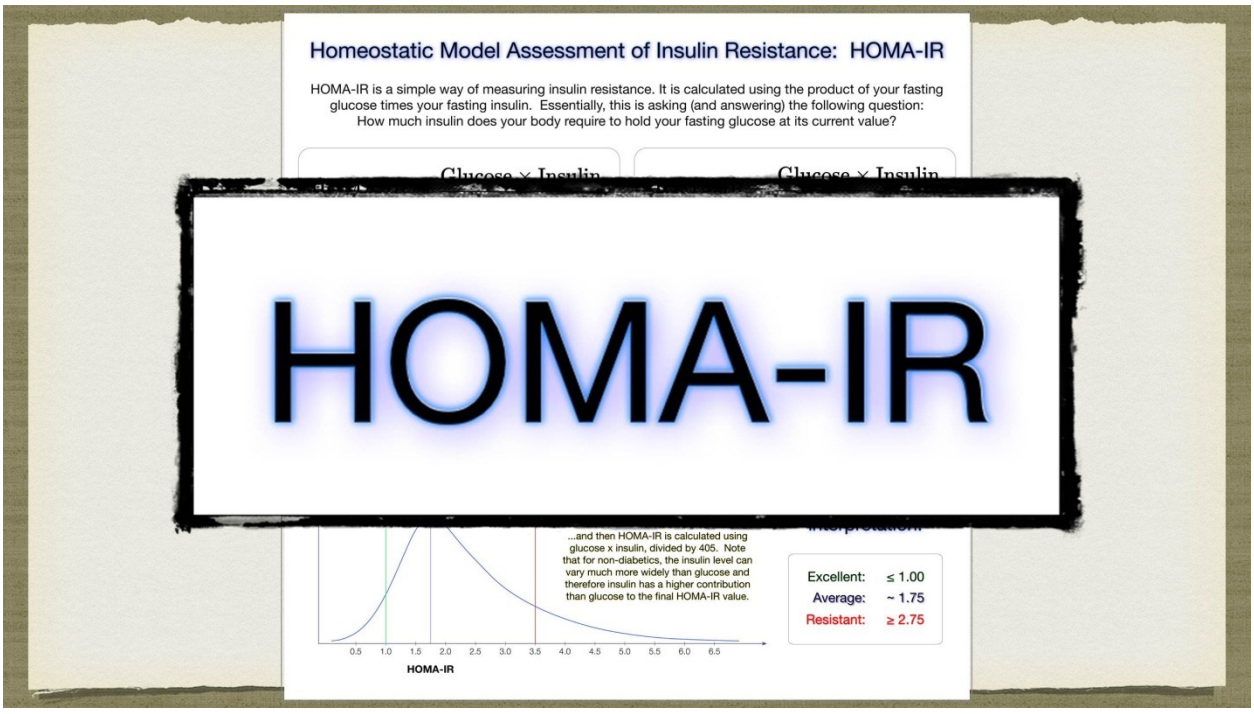
VIDEO_ Ted Naiman - Presentation (Breckenridge 2017)

Dr. Naiman: Did anyone catch the CrossFit Greg Glassman talk last year where he talked about the five buckets of death? It turns out that anytime somebody dies, that could be categorized as one of five things. You've got up in the top right-hand corner 30% of deaths is toxic kinetic microbial genetic.

But down in this giant 70% of all deaths you've got chronic disease. And of course a big three - cancer, cardiovascular disease and chronic neurodegenerative diseases like Alzheimer's. What we know about all these chronic diseases that is driven by sedentation and malnutrition, this is poor diet and lack of exercise and underpinning all of this stuff is insulin resistance.

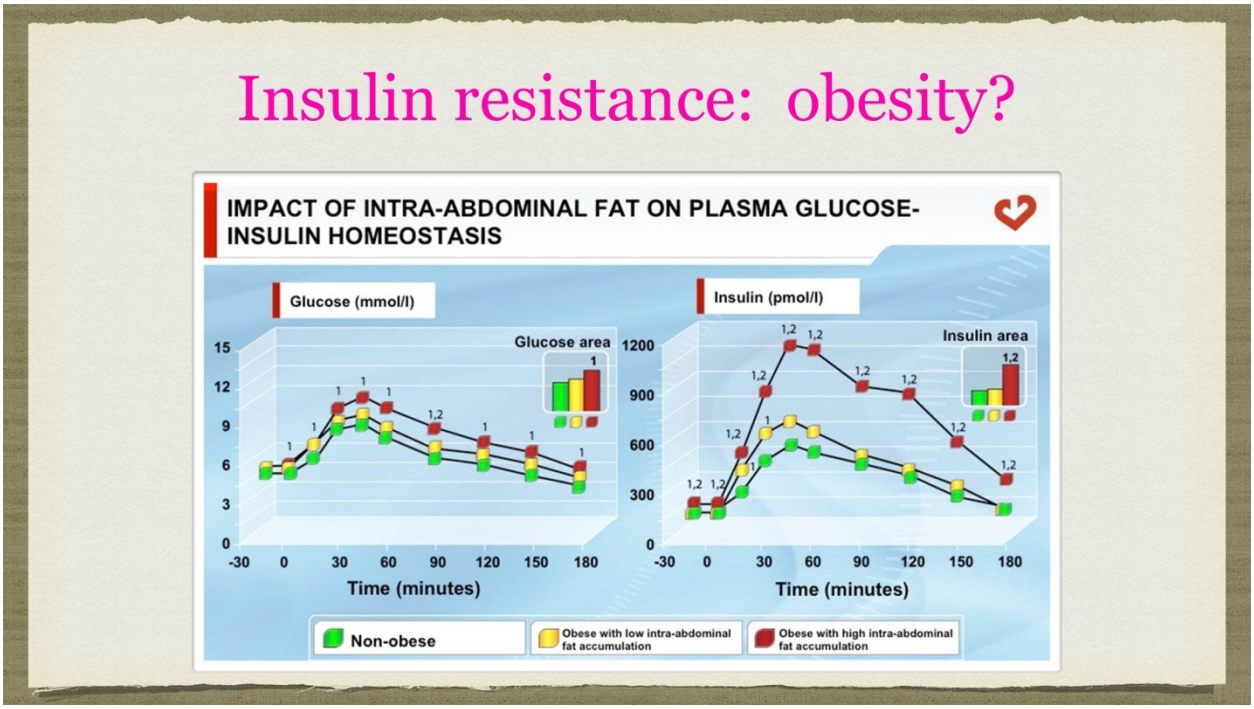
And that is why this is such a huge big topic. I mean I will never stop talking about this because it's really that important. I just want to say at the top of my talk here that I use HOMA-IR with a lot of my patients these days. This is homeostatic model assessment of insulin resistance.



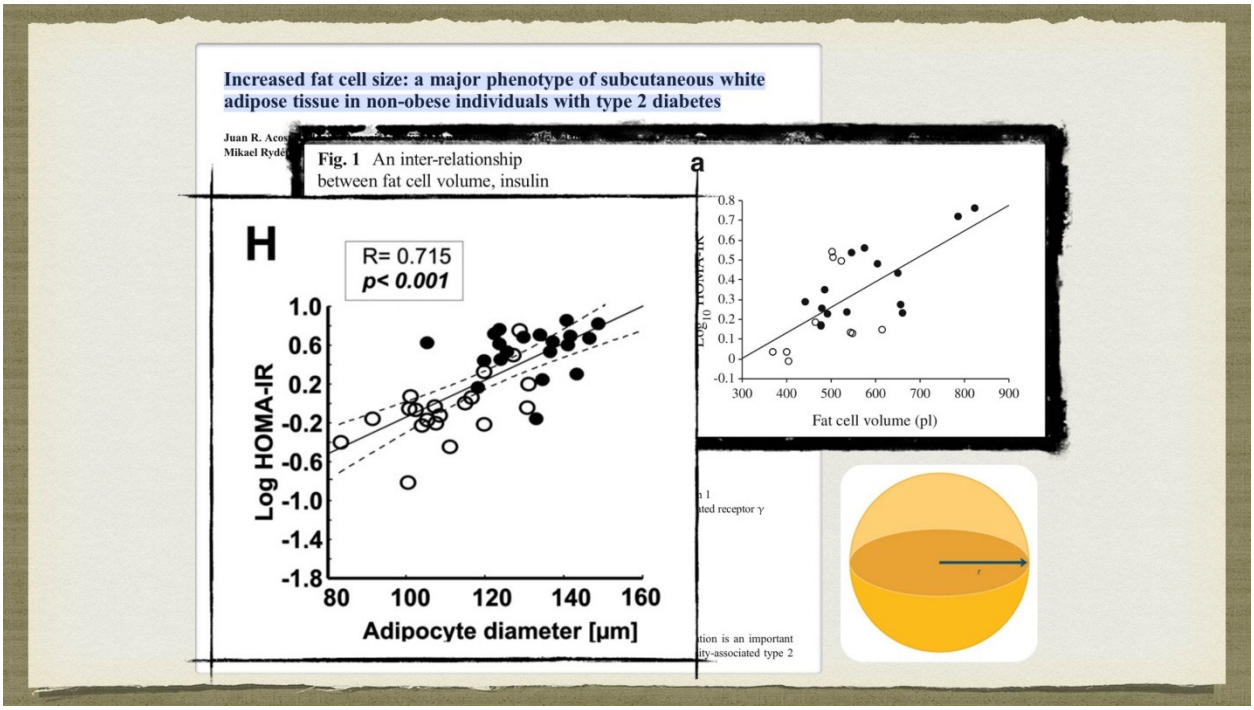
This is my favorite way to noninvasively measure insulin resistance in my patients. This is something you'll see most commonly in the medical literature when people are looking at insulin resistance. It's really just your fasting glucose times your fasting insulin divided by 405. And it's answering the question, "How much insulin does it take when I'm fasting to hold my blood sugar and my fat stores where they are at right now."

The average in this country is 1.75, that's really a little too high. You want to be a 1.0 or lower. Anything over about 2.5 is clearly insulin resistance. You could just search the medical literature for HOMA-IR in any chronic disease you can think of, and it's just a huge linear association. HOMA-IR in cardiovascular disease, huge linear association, dying of heart attacks, huge association, cancer, huge association...

All forms of cancer, huge association, I mean it's just ridiculous. Alzheimer's pathology, massive association with insulin resistance. And finally just dying. All cause mortality and HOMA-IR - big association there too. So this is a really important topic. Okay so now what causes insulin resistance? What we've known forever that the more abdominal fat you have the more insulin resistant you are. This graph on the right shows insulin levels.



You've got normal in green, obesity in yellow and abdominal obesity in red. So we've known that for a long time, right? But what about this? Here is a graph of insulin sensitivity versus body mass index. And how do you explain these people way down here? They've got a BMI less than 20, but their insulin sensitivity is terrible. I mean, what's going on here, right? Well, we've known for over 50 years that the larger your adipocytes the more insulin resistant you are. And in fact it's a perfectly linear association.



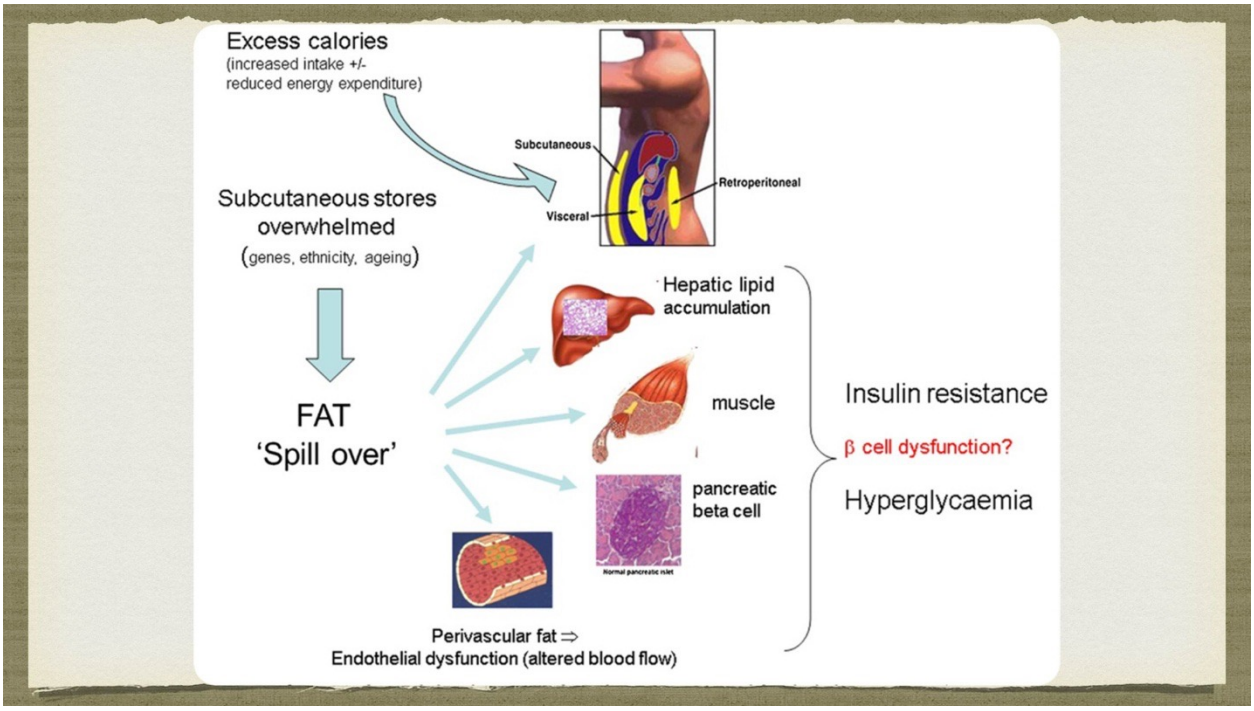
Your adipocytes can expand in diameter about 20 times. So if you look at a cross-section of adipocytes in a microscope, they can go from maybe 10, 20 µ to 200 µ. That means their volume can expand by 8000 times. And as a get bigger, they get more insulin resistant and it's very, very linear. It turns out that our large adipocytes are resistant to the antilipolytic effects of insulin and it's harder to shove more fat in there, right? You can graph out fasting insulin, HOMA- IR, any marker... metabolic syndrome... it's perfectly linear with adipocytes size.

Triglycerides go up, HDL goes down, HOMA-IR goes up, insulin goes up. Any metabolic syndrome or insulin resistance marker you measure will completely correlate up or down linearly with the size of your adipocytes. If you have gastric bypass surgery and you manage to shrink the size of your adipocytes, you'll reverse insulin resistance and diabetes. If you lose weight with any mechanism, it's more important how much you shrink your adipocytes rather than how much weight you actually lose in terms of reversing insulin resistance.

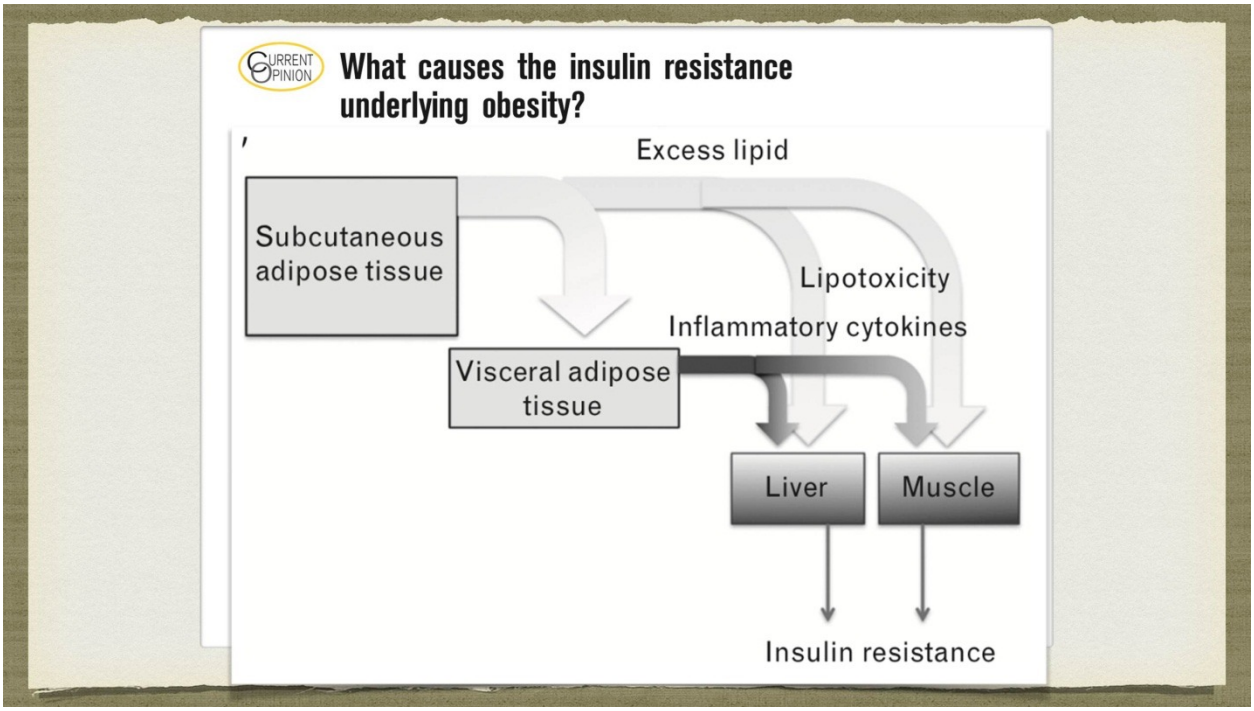
And that's why people can reverse insulin resistance really rapidly even before they lose a whole lot of weight. It turns out that has you get fatter your fat cells can do one of two things; You can have adipocyte hypertrophy and that's where your fat cell gets overstuffed with fat and it's inflamed and it's insulin resistant and it doesn't want any more fat or glucose, or you can have adipocyte hyperplasia. If you have the right genetics, you can sprout cute new little baby fat cells that are very insulin sensitive and they're happy to suck up more fat and they're not inflamed, they're not insulin resistant.

So not all your fat cells are alike, right? Your enormous huge overstuffed fat cells are super inflamed, they're sick, they're dying, they're spewing out fat constantly. It takes a crap ton of insulin to shove fat in there. The fat doesn't want to stay in there, but your cute little baby fat cells are very insulin sensitive and they're more than happy to suck up more fat flux, right? So you can have two people of identical obesity and the person who has overstuffed their fat cells and had adipocyte hypertrophy is going to be inflamed and insulin resistant and it takes a ton of insulin to shove anymore fat in there and the fat is constantly spewing back out.

But somebody who can sprout new little baby fat cells is going to stay insulin sensitive forever. If you have the right genetics and you can just sprout new fat cells as hyperplasia you could be 600 pounds and as long as you have some small fat cells around that still suck up more fat you're going to be totally insulin sensitive. This is about 10% of obese people. So there is this concept of limit of adipose tissue expansion. Basically there's a limit to how easily you can get fatter either by sprouting new baby fat cells or expanding the little ones you've got. And once you've hit this limit, you're insulin resistant. So fat is typically stored in subcutaneous first and then it spills over into visceral and then it spills over into liver and muscle and pancreas and blood vessels.



And you've got ectopic fat and you've got fat everywhere and you're horribly insulin resistant. Here's a sort of a schematic of how it works.



You fill up your subcutaneous adipose first, it spills over into visceral, that spills over into liver and muscle and now you've got ectopic fat and none of your tissues want any fat or glucose and now you're insulin resistant. My favorite term when it comes to this concept is "personal fat threshold" or PFT. This is a genetic limit to how fat you can get before you just can't get fatter and insulin resistant.

This explains people who are tofi, thin on the outside, fat on the inside. I think Dr. Berger mentioned that. And these are people who look thin, but they've completely maxed out their fat source subcutaneous and visceral and are horribly insulin resistant or maybe completely diabetic. This is why China and India have passed up diabetes prevalence compared to US at a much lower body mass index, personal fat threshold.

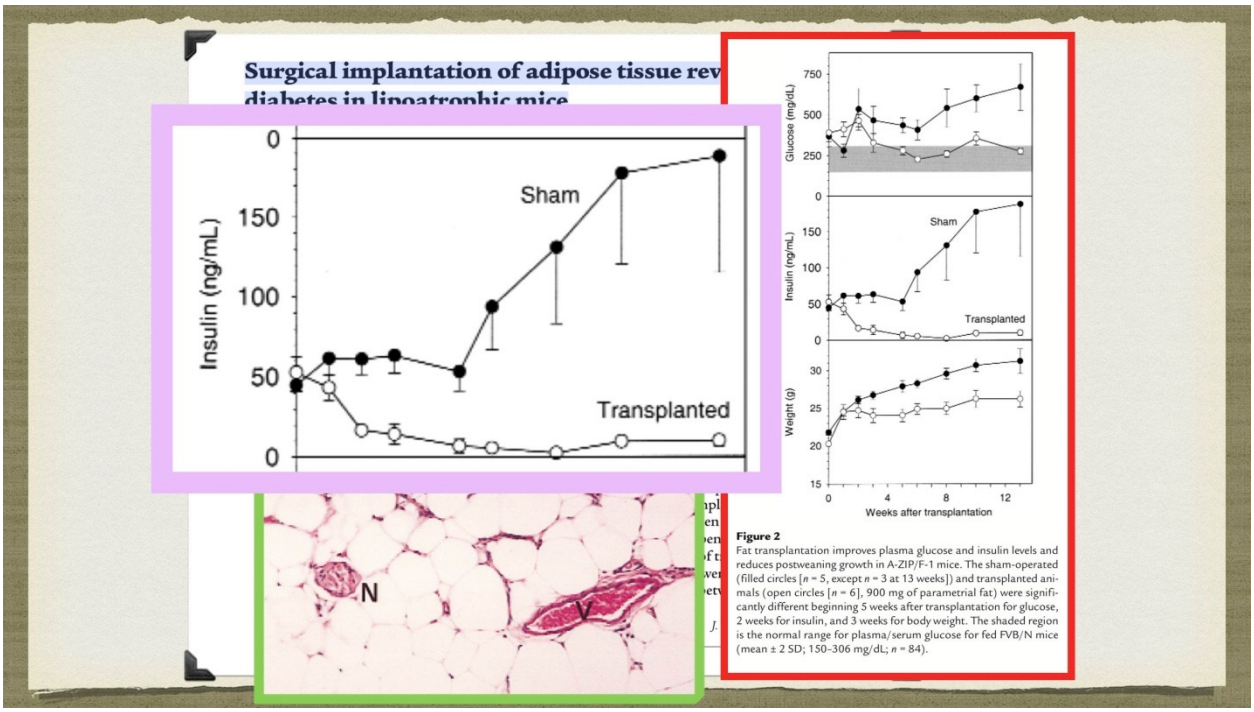
And this slide is here to remind me that your giant overstuffed hypertrophy fat cells are literally dying. These great things on the right are dead adipocytes and that's why you have so many macrophages. These cells are not happy, they're sick, they're dying, they're inflamed. The little baby fat cells are happy as clams. I love this graph right here. It takes a ton of insulin to shove that much fat into an adipocyte and hold it there and to pin it there tonically. And that fat is constantly trying to spew back out. And that's why people who have maxed out their fat cells just have high insulin 24/7. This is a beautiful illustration. The best example we have of adipose tissue controlling insulin resistance is lipodystrophy.

Lipodystrophy is a series of disorders where you don't have any subcutaneous fat, or hardly any. I have a bunch of patients with lipodystrophy. They're very unique and they almost looked ripped like a bodybuilder. They have very defined arms and legs, they have very little

subcutaneous fat, but they have a lot more visceral fat than you would expect. If you do cross-sectional imaging on these people, the subcutaneous fat in red here is very, very small, but the visceral fat is completely maxed out.

And almost everyone with lipodystrophy has horrible insulin resistance and horrible brittle diabetes. All my lipodystrophy patients have really bad diabetes. It is the worst insulin resistance. Now you can buy a mouse that has lipodystrophy right? We found mice that lack subcutaneous fat for whatever reason and we've bred them. And you can actually buy and sell lipodystrophy mice and it's a great model for insulin resistance and diabetes, because no matter what you feed them, they just completely max out subcutaneous fat, it all goes to visceral fat, they have fatty liver, they have visceral fat, they're insulin resistant, diabetic just like humans.

And we did this amazing study on these lipodystrophy mice where we literally surgically implanted little pouches of subcutaneous fat under their skin and connected to blood supply and you instantly magically cure insulin resistance in these mice. Look at this black line on top - that's that sham surgery.



And you're looking at insulin levels versus fat transplant surgery on the bottom in white. You literally, instantly, magically cure insulin resistance in these mice, by just implanting fat under their skin. This is kind of the final nail in the coffin of anyone who doesn't buy into the theory that adipose controls insulin resistance. We haven't done this exact study in humans, I don't think people would really like that, but we do have glitazones.

Glitazones is a classic diabetes drug that enables you to get a little bit fatter. They don't work that great, you get a little fatter and your insulin resistance and diabetes gets a little bit better. I don't like that. If patients knew how it worked, they probably wouldn't want to take it. Okay, so here's how it works so far.

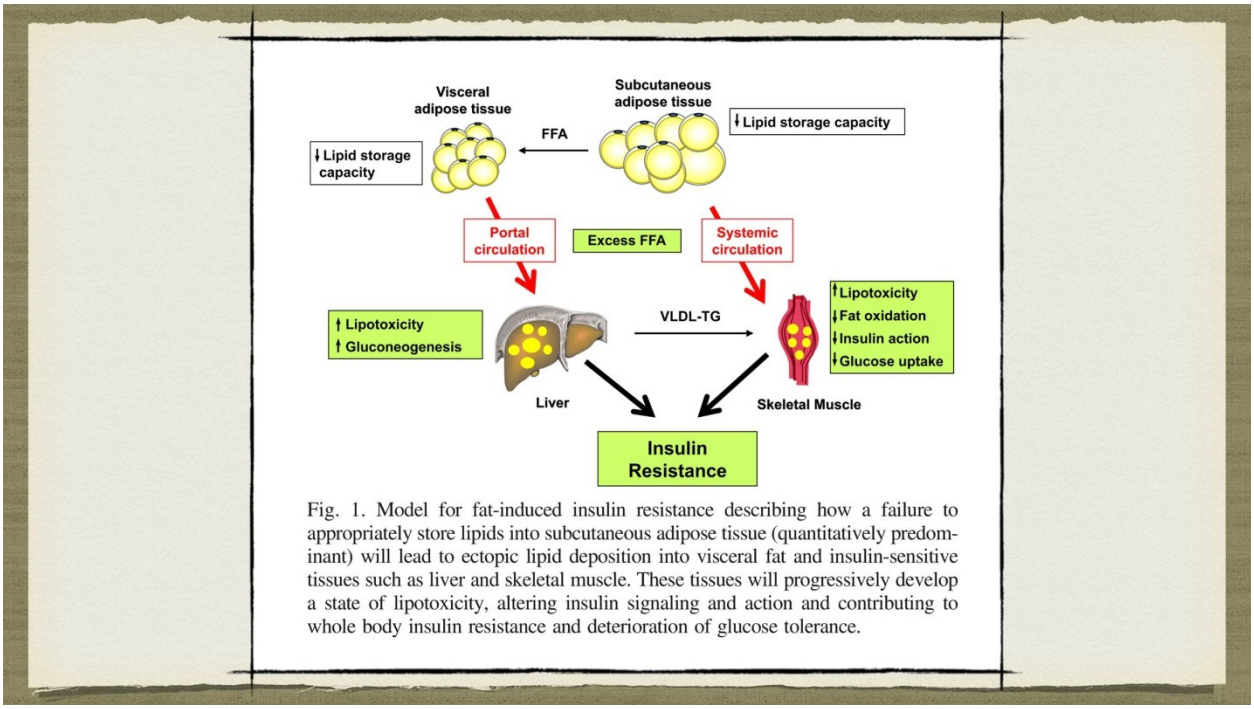


Fig. 1. Model for fat-induced insulin resistance describing how a failure to appropriately store lipids into subcutaneous adipose tissue (quantitatively predominant) will lead to ectopic lipid deposition into visceral fat and insulin-sensitive tissues such as liver and skeletal muscle. These tissues will progressively develop a state of lipotoxicity, altering insulin signaling and action and contributing to whole body insulin resistance and deterioration of glucose tolerance.

You fill up your subcutaneous fat, then it spills over into visceral, that spills over into liver and muscle. Now you've got ectopic fat, you've got fat everywhere. None of your cells wants fat, none of your tissues wants fat, you're insulin resistant. What's really going on here is your body is at war with itself. None of your cells wants fat, none of your tissues wants fat, none of them wants glucose either, none of them wants any of this energy and it's like this horrible game of musical chairs, where insulin just gets louder and louder and louder until you finally shove some fat or glucose into whatever so our tissue is the least insulin resistant and next time it'll probably be even more insulin resistant.

And once your body is at war with itself like this, the wheels just fall off your wagon and this is why all of these chronic diseases are driven by insulin resistance. Okay, bottom line so far... You are insulin resistant because you filled up all your adipocytes. You have no more room for fat flux and every time you eat a meal, it has nowhere to go, the fat, or the glucose. So you're just completely filled and that's where you're insulin resistant and that's where you're hyperinsulinemic and you have high insulin al the time.

But this is just the beginning. I mean the big question is, "Why did you fill up your adipocytes?" Why are they all full? Because humans should need fat because we should be low-fat vegans. Is it because you're just a gluton and you eat too much, right? No, you filled up your fat cells with fat because you suck it burning fat because you eat too much glucose. "An important contributing factor for obesity is reduce fat oxidation "and increased metabolism of carbohydrate. This has been brought about by a shift toward oxidizing carbohydrate rather than fat resulting in an increased deposition of body fat."

You're eating carbs and glucose, you're not burning fat. It accumulates, you fill up your adipose. Turns out everybody with obesity, insulin resistance, ectopic fat has defects in mitochondrial metabolism of fat. Everyone in this situation has trouble metabolizing fat in the mitochondria. Obesity, insulin resistance, type 2 diabetes and aging all associated with impaired skeleton muscle oxidation capacity reduce mitochondrial content and lower rates of oxidative phosphorylation. Basically you are not burning fat in your mitochondria.

"Mitochondrial mass, structure, function are altered in insulin resistance. Defects of mitochondria are believed to contribute to impaired fat oxidation and to the accumulation of intramyocellular lipid intermediates, which contribute to the pathogenesys of insulin resistance. Mitochondrial dysfunction in the elderly and in the offspring of diabetic patients is well-documented" So basically you're not burning fat well. It accumulates, you fill up your adipose. Now only your mitochondria can oxidize fat, it's all happening in the mitochondria.

And let's talk about that for a second. Every nucleated cell in your body has mitochondria in it, right? And they're just constantly turning your food into ATP, which drives everything in your body. And the turnover rate is just enormous. Every single day you make your entire body mass in ATP molecules. If you're a 70 kg male you manufacture 70 kg of ATP molecules every day, which is ridiculous.

The turnover is so fast that at any given second in time you only have six seconds of ATP left in your body. In fact that is what cyanide does. Cyanide poisons your electron transport chain, you can't make ATP and you're dead six seconds later. So these suckers are constantly performing metabolism. And there are three things going into the cell that your mitochondria can burn; Glucose, FFA, free fatty acids, that's just fat, or amino acids.

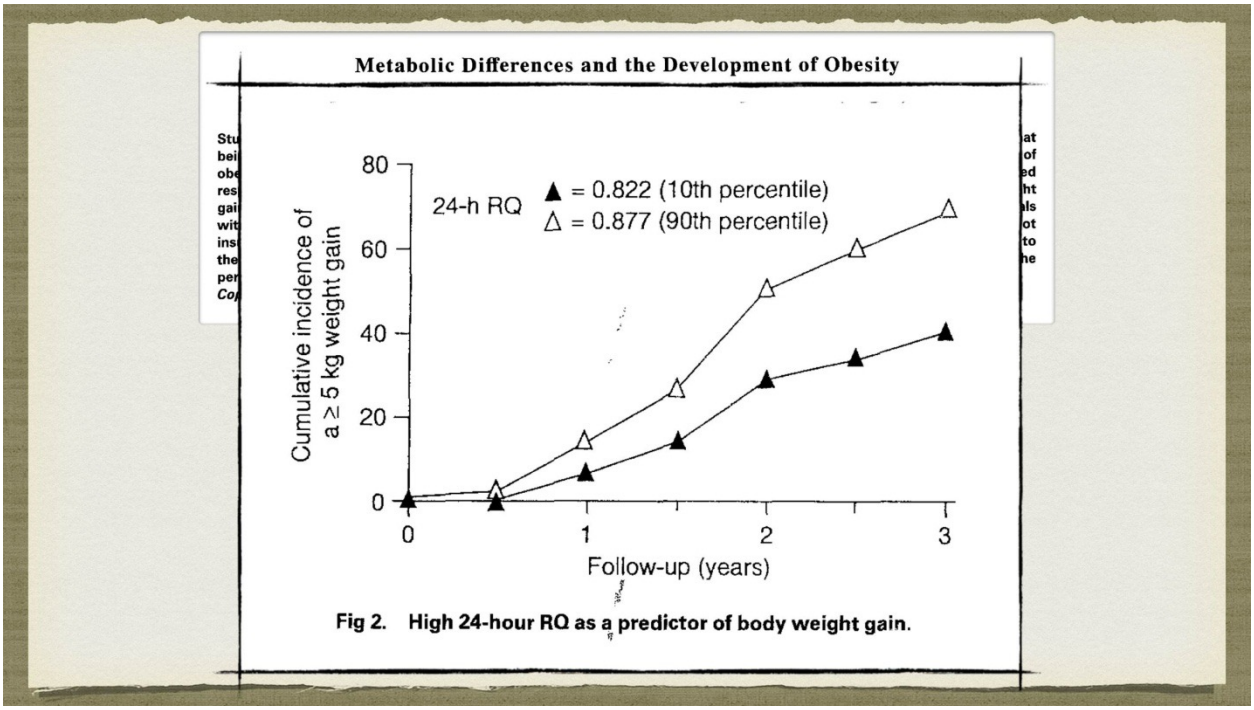
Now amino acids are a sort of a minor player. Most of the time people are oxidizing glucose or fat. And glucose and fat are oxidized reciprocally. So anytime you're burning more glucose, you're burning less fat and more of fat and you're burning less glucose. Now you can actually tell what the fuel mixture is in every mitochondria in every cell of your body by measuring your respiratory quotient, right?

You actually breathe out a lot more carbon dioxide if you're burning glucose in your mitochondria than if you're burning fat. You breathe out less carbon dioxide and because

they're reciprocal, you can actually calculate it out. If you have the highest respiratory quotient of 1.0, you're breathing out the most carbon dioxide and you're burning pure glucose in all your cells, all your mitochondria.

If you have the lowest respiratory quotient of 0.7, you're burning pure fat and you're making the least carbon dioxide. And because it's reciprocal you can just look at that line and tell exactly what your film extra is based on your respiratory quotient.

The fascinating thing about respiratory quotient is you could take two people in this room and measure their baseline respiratory quotient and whoever has the higher one meaning they're burning more glucose and less fat at baseline will literally be significantly fatter three years down the road. That's what this study was.



Measure based on RQ, whoever's burning more glucose and less fat is literally going to be fatter later. "The effect of fat oxidation remains..." Yeah, I couldn't agree more. It turns out you can take two people of the same obesity. Whoever has the higher or whoever has the lower respiratory quotient, meaning they're burning more fat, is going to be metabolically healthier.

They're going to have lower insulin, less metabolic syndrome. If you're insulin resistant, you have a higher RQ. If you're diabetic, you have a higher RQ, if you're obese, you have a higher RQ, if you have a family member with diabetes, you have a higher RQ. Anything bad metabolically you have a higher RQ and that's just not good.

There's also this concept of "metabolic flexibility". Metabolic flexibility is the ability to drop your RQ if you're eating more fat. So if I'm thin and healthy and I have tons of really good mitochondria and I am good at burning fat, if I eat a high-fat diet I will immediately drop my RQ and burn more fat.

Also if I'm fasting and I'm just living off of fat, my RQ goes way down. People with poor metabolic flexibility can do that. If they eat a higher fat diet they end up just storing that. If they are fasting they struggle to meet their metabolic needs just from fat. You can draw a graph of metabolic flexibility and insulin sensitivity and it's just a straight line, right?

Now, okay this is a really important point. If you are on a mixed diet and you eat a bunch more carbs you will immediately raise your RQ. And anybody, you can drive up anyone's RQ by feeding them more carbs and glucose, because glucose completely controls metabolism and substrate oxidation. It has to because you don't have anywhere for that glucose to go. So if I feed anyone more carbs their RQ goes up.

The same isn't true on a mixed diet. If you're eating just a regular standard American diet and you add more fat to it, you just throw a stick of butter on top you will not drop your RQ, you'll just store all that butter.

I'm reading in this box here, "Excess carbohydrate results in increased carbohydrate oxidation, "a lower fat oxidation, increased RQ. "This is not the case for fat. "Excess fat intake on a mixed diet does not stimulate fat oxidation, but enhances fat storage."

That's because glucose rather than fat completely controls substrate oxidation. Glucose controls oxidation and here's why glucose has to control metabolism and substrate choice.

Professor Flatt drew this diagram, this hydraulic mechanical model of metabolism like 60 years ago.

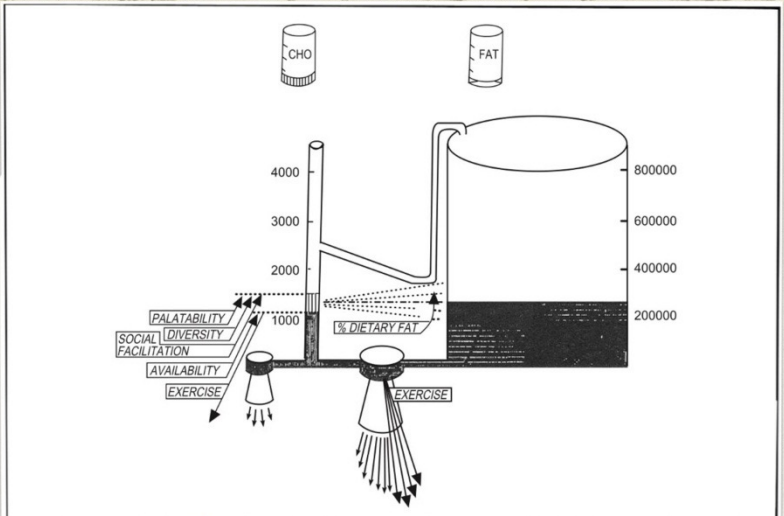
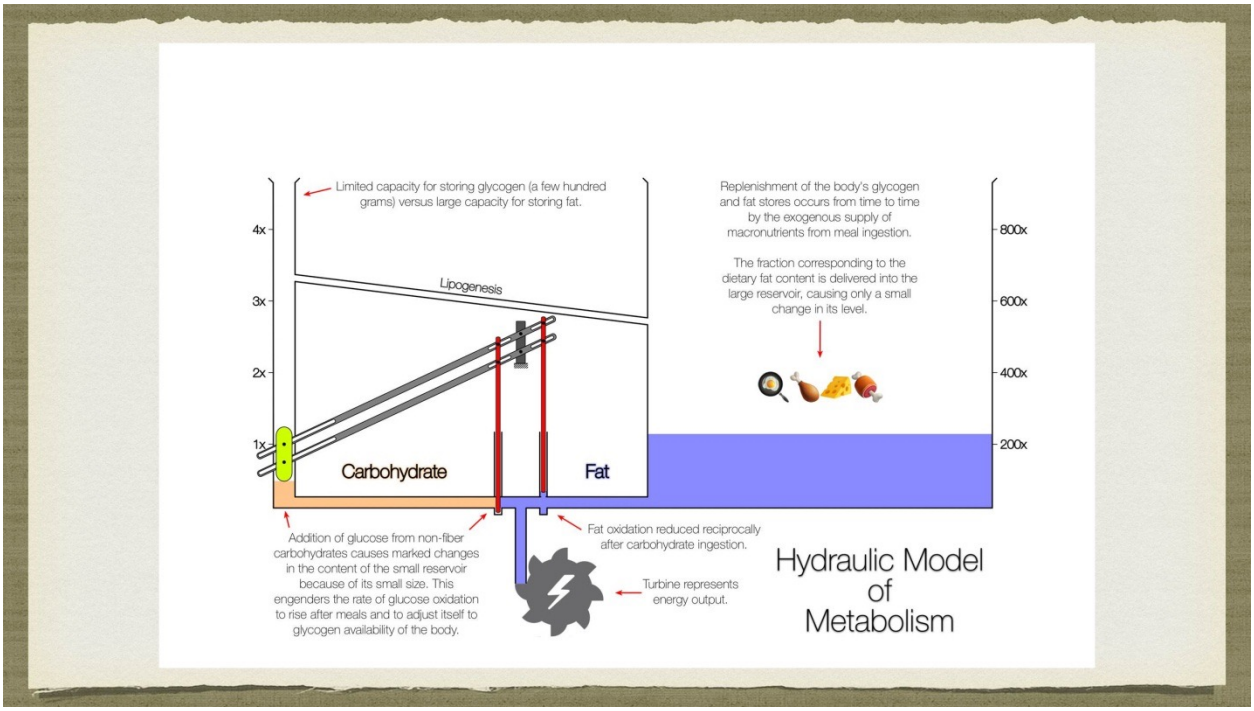


Fig. 4. Hydraulic model of Flatt [9,10], which is constituted by 2 reservoirs, a small and large one, describing that limited capacity of the body for storing glycogen (a few hundred grams) and the large capacity for storage fat (a few decakilos), respectively. There is a small turbine, which represents the exclusive use of glucose by the brain (approximately 100 g/day). The relative proportions of glucose and fatty acids used by the body (brain excluded) is represented by the large turbine and is assumed to be influenced by the proportional availability of glucose and free fatty acids. Replenishment of the body's glycogen and fat stores occurs from time to time by the exogenous supply of macronutrients (meal ingestion). The fraction corresponding to the dietary fat content is therefore delivered into the large reservoir. Addition of fuel from the meals to the large reservoir cause only a small change in its level, whereas marked changes in the content of the small reservoir occurs because of its small size. This engenders the rate of glucose oxidation to rise after meals and to adjust itself to glycogen availability of the body.

And you've got this giant fat reservoir over here on the right. That's 200 times bigger than this tiny little glucose carbohydrate reservoir. So when I dump a bunch of fat into the system, nothing has to change. I don't have to change my fuel mixture I can do that all day long.

On the other hand you only have a tiny little carb glucose reservoir. It's really small. You can have 5 g of glucose in your blood stream, maybe a couple of hundred grams in your liver and your muscle and that's it. So when you dump in a bunch of carbs and glucose you literally have to switch your metabolism over and burn more glucose.

I've made a fancier little hydraulic model metabolism here.



And again you've got a fat reservoir on the right so when you dump more fat in nothing has to change. But as you add carbohydrates and raise glucose, you literally have to switch your metabolism over and burn more glucose just to get rid of it. You just have no other choice, that's how it has to work. In fact if you eat enough carbohydrates and glucose, you literally have to convert it to fat via De Novo Lipogenesis to store it and get rid of it. Only when carbohydrates and glucose are absent can you switch your fuel mixture over and burn fat again.

There's another concept here, that's "glucose hysteresis". There's an inertia of your metabolism. "A general feature of metabolic regulation is that substrates typically induce the metabolic machinery necessary for their own metabolism" What does that mean? If you're good at burning fat you have epigenetic changes that up regulates your fat burning pathways and you'll stay good at burning fat for a period of time. It's like an inertia to your memory, to your metabolism.

On the other hand if you're a glucose burner, you have epigenetic changes, you up regulate your glucose burning and you sort of stay good at that. That's why it takes, you know, one to three weeks to switch over from a high carb diet to a low-carb diet. Okay this this study sums it up so I'm just going to quote directly from it. "The development of insulin resistance "is the impaired ability of skeletal muscle to oxidize fatty acids "as a consequence of elevated glucose oxidation "in the situation of hyperglycemia and hyperinsulinemia. "and the impaired ability to switch easily between glucose and fat oxidation "in response to homeostatic signals.

"The decreased fat oxidation results into the accumulation of intermediates of fatty acids metabolism..." Basically there's so much carbs and glucose around, you can't burn fat, the fat

accumulates, now you're insulin resistant. This concept of metabolic flexibility goes all the way down to the mitochondrial level. So here's your mitochondria with the two inputs - glucose and fat. And a healthy mitochondria can easily flex back and forth, glucose, fat, glucose, fat. But if you have an inflexible mitochondria, one of these damaged mitochondria, it's really bad at doing that, it really struggles.

What's going on inside your mitochondria? As you've got glucose and long chain fatty acids, the two input into the cell, glucose and fat... Glucose goes into the mitochondria and when you dump in a bunch of extra glucose you have increased citrate. And citrate gets exported to the cell. And because there's extra citrate, your body knows it's time to make fat instead of burning fat. So your cell is going to make fat, it converts it into Malonyl-CoA. That literally blocks CPT-1 and fat actually physically cannot enter your mitochondria to be burned, when Malonyl-CoA is elevated.

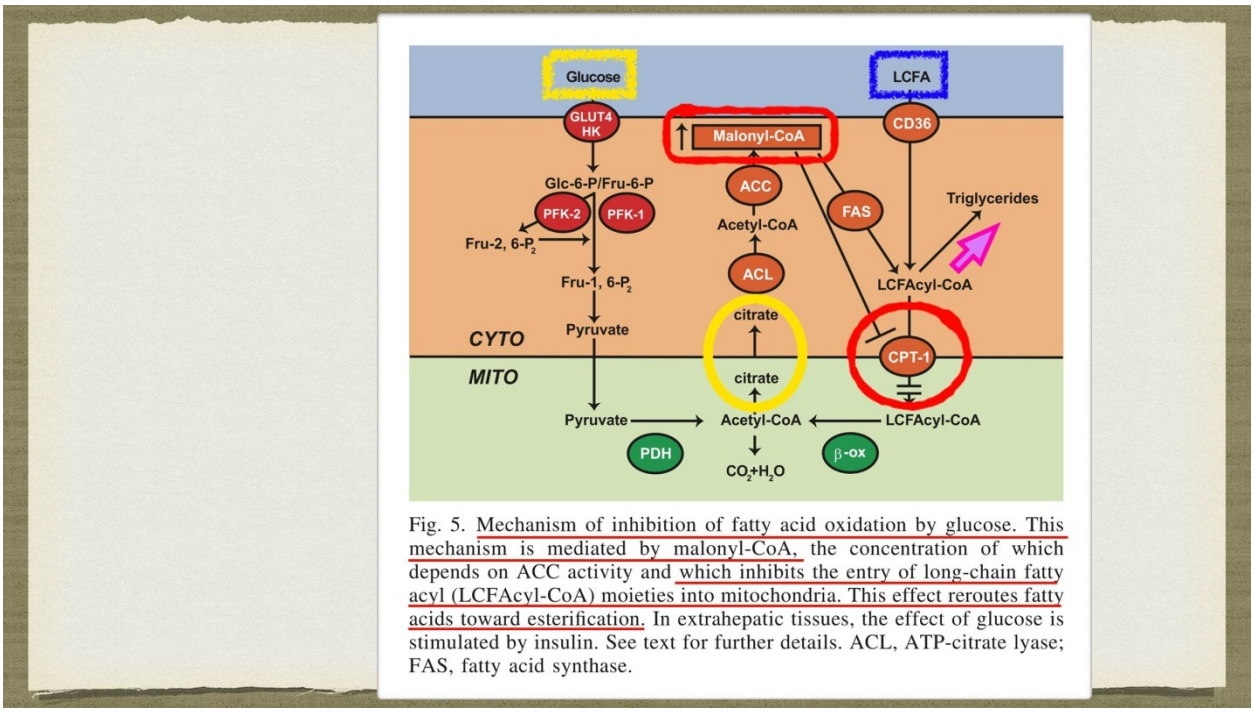


Fig. 5. Mechanism of inhibition of fatty acid oxidation by glucose. This mechanism is mediated by malonyl-CoA, the concentration of which depends on ACC activity and which inhibits the entry of long-chain fatty acyl (LCFAcyl-CoA) moieties into mitochondria. This effect reroutes fatty acids toward esterification. In extrahepatic tissues, the effect of glucose is stimulated by insulin. See text for further details. ACL, ATP-citrate lyase; FAS, fatty acid synthase.

In other words, when you're making fat you don't want to burn fat. That would be wasteful. So all your fat is rerouted as triglycerides to be stored. I'm reading the caption here... "Mechanism the of inhibition of fatty acid oxygen by glucose..." Basically Malonyl-CoA inhibits the entry of long chain fatty acids into the mitochondria. This effect reroutes fatty acids towards esterification. So when there is a bunch of glucose present you can't burn fat. Here is another illustration of the same thing.

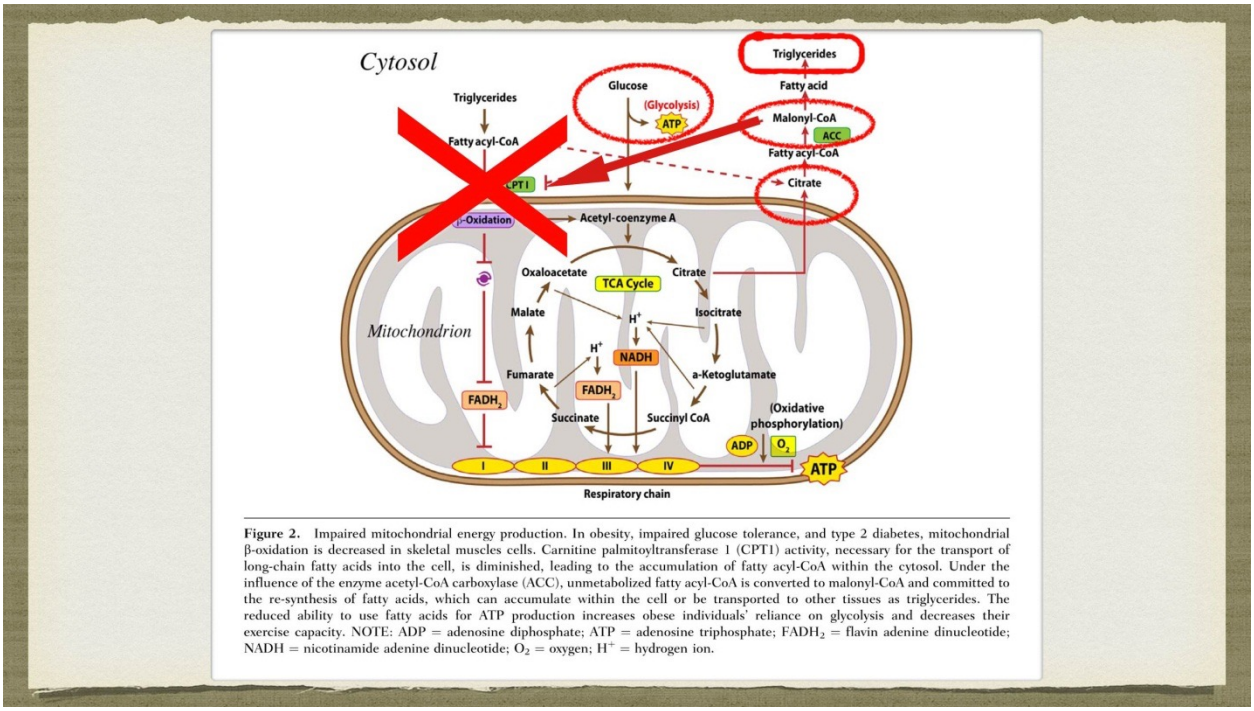
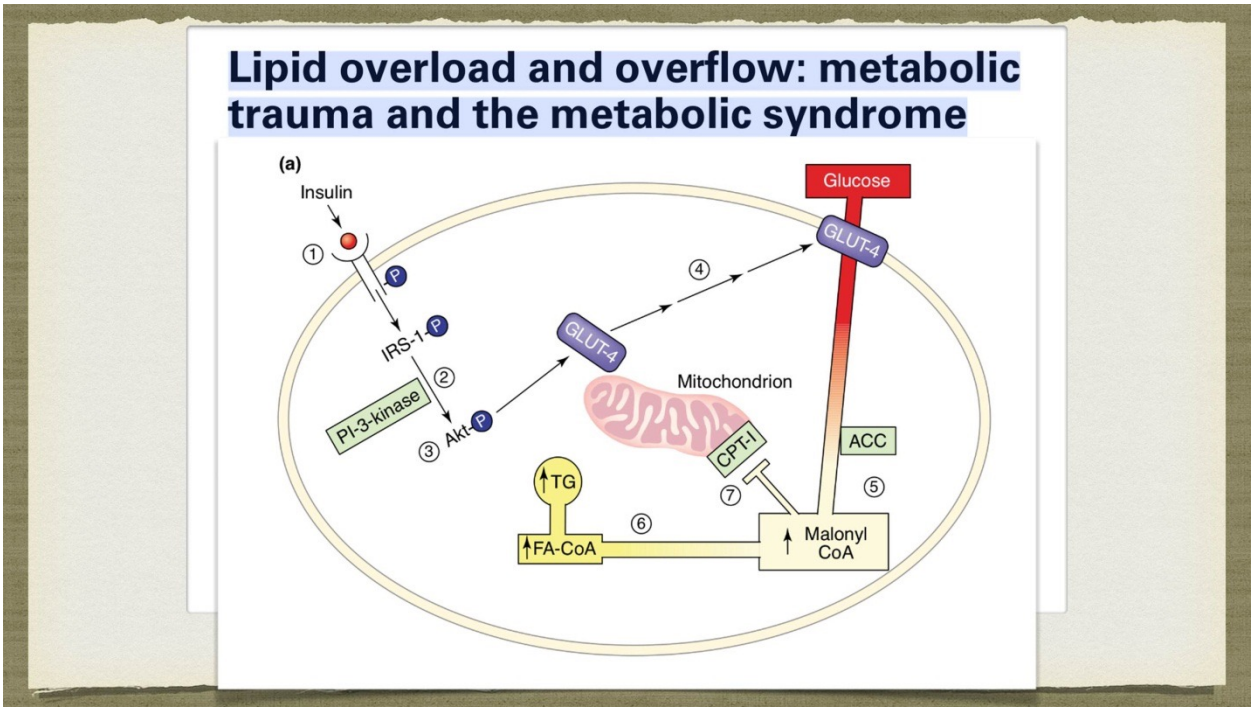


Figure 2. Impaired mitochondrial energy production. In obesity, impaired glucose tolerance, and type 2 diabetes, mitochondrial β-oxidation is decreased in skeletal muscles cells. Carnitine palmitoyltransferase 1 (CPT1) activity, necessary for the transport of long-chain fatty acids into the cell, is diminished, leading to the accumulation of fatty acyl-CoA within the cytosol. Under the influence of the enzyme acetyl-CoA carboxylase (ACC), unmetabolized fatty acyl-CoA is converted to malonyl-CoA and committed to the re-synthesis of fatty acids, which can accumulate within the cell or be transported to other tissues as triglycerides. The reduced ability to use fatty acids for ATP production increases obese individuals' reliance on glycolysis and decreases their exercise capacity. NOTE: ADP = adenosine diphosphate; ATP = adenosine triphosphate; $FADH_2$ = flavin adenine dinucleotide; NADH = nicotinamide adenine dinucleotide; O_2 = oxygen; H^+ = hydrogen ion.

You dump in a bunch of glucose you export citrate, Malonyl-CoA first committed step to making fat. So you don't want to burn fat and you block entry of fat into the mitochondria and all your fat accumulates as triglycerides to be exported and stored. What's really going on here is your body is way too efficient to make fat and burn fat at the same time. So when you dump a bunch of glucose into your cell, your body knows it's going to make fat, fatty acid synthesis and Malonyl-CoA is the first committed step to fatty acid synthesis, blocks CPT-1.

Because you don't want to be making fat on one side and then burning fat on the other side. That would just be a futile cycle, your body is not going to do that. That's why glucose and fat are burned reciprocally all the way down at your mitochondrial level, because when you're burning glucose and you're going to be making fat you don't want to be burning fat. We've proven that this happens. Here's a brilliant study that literally proves this. They measured oxidation of glucose and fat in the mitochondria baseline.

They infused people with glucose and insulin and immediately glucose oxidation goes way up, fat oxidation goes way down. That this is just how it works, this is why if you eat carbs all day long you're not burning any fat at all. "Intracellular availability of glucose, not fatty acids, "is the prime determinant of the substrate mix IE glucose versus fat, that is oxidized for energy." In other words you dump in glucose you literally have to burn glucose not fat. That's just how the whole system works. Here's a cuter picture of it.



Insulin binds to the cell on the upper left-hand corner, the glut for transporter goes to the service, glucose comes in, it's converted to Malonyl-CoA because you'll turn it into fat, so that blocks CPT-1, so you don't burn any fat and then all your fat accumulates there in yellow. Now let's say I eat just a diet of pure glucose. I'm some crazy low-fat vegan and all I eat is just sugar. I'm on a sugar diet, I'm on some sort of Kempner Rice Diet... Okay I only eat glucose, but I don't overeat and I'm careful with calories. Yes, I'm blocking the entry of fat into the mitochondria, but I don't eat any fat so fat isn't accumulating.

I actually won't gain weight. You could eat a diet of pure sugar and you will not gain weight. You're horribly locked into glucose dependence, so I don't recommend it at all. If I dump a bunch of butter on top of that, oh yeah then I will gain 1000 pounds. Because you're blocking the oxidation of fat with all the glucose and then all the fat accumulates and the next thing you're insulin resistant. In fact what happens is your cell sees what's going on here, all this fat that's accumulating and the accumulated fat shuts off insulin signaling, so the GLUT-4 transport goes back inside the cell and your cell is refusing glucose.

Your cell doesn't want any more glucose with all this fat that is accumulated. Your cell doesn't want glucose, right? Your cell is smarter than you are. What could you do with your diet when your cell doesn't want more glucose? I can't think of anything, but... Now if we take it even one layer deeper and look at the electron transport chain, which we saw earlier thanks to Dr. Eades, so you're pumping all these protons across this membrane, it's like a little battery that powers your ATP synthase motor and it spring loads all your ATP molecules...

When you're just doing beta oxidation of fat everything runs really smoothly. You're level loading your electron transport chain, the membrane potential is perfect, everything is nice... Your body is designed to just live off of stored body fat, so just burning fat has to work perfectly. Now you dump a bunch of glucose on top of this and you overdrive Complex 1 and you get too much membrane potential and too many reactive oxygen species and you literally get something called glucose toxicity in your mitochondria.

You can basically bust those suckers by trying to burn sugar on top of beta oxidation. Okay let's take this into the real world. Here is a company that specializes in obesogenic rat chow. This is what they do, they make an obesogenic rat chow that people pay money for this stuff. It's supposed to make you as fat as possible, as fast as possible. I'm talking visceral obesity, liver fat, insulin resistance, diabetes, the whole thing.

This obesogenic rat chow is very low in protein, it's high in fat and carbs, it's really high carb if you look at the grams, it's vaguely eerily similar to the standard American diet. It's pretty sad, right? So we know how to make both animals and humans as fat as possible as rapidly as possible... is sugar and fat together, right? The obesogenic rat chow is a refined, processed, concentrated fat and sugar mixed together. It's usually cornstarch and vegetable oil or something like that. But it's low in protein, low in nutrients, it's just sugar and fat. And that's how you get anything as fat as possible as rapidly as possible.

You can feed humans donuts, it's pretty much the same thing. So we know how to get the highest insulin levels, the most overfilled adipocytes, the worst body composition, the highest fat mass, the lowest lean mass; You do that by feeding high carb and high-fat and you keep everything else low. Sugar and fat, this is the absolute worst. We also know how to get your adipocytes the very smallest and how to get the very lowest insulin levels. And we know that thanks to natural bodybuilders and fitness models and esthetic athletes and they accomplish this by either going...

Well they usually go high in protein, very low-carb and sort of low-ish in fat. We have studies that document how this is done. This is female fitness competitors, they achieve this low body fat reducing carbohydrate intake while they maintain a high-level protein, resistance training and moderate fat. So it's basically very low-carb, high-protein, moderate fat and lifting. So we also know what calories got dumped into the American diet to cause the obesity epidemic over the past six years. Grains, oils and sugar.

This is flour, sugar and oil, or as I call it, "The processed food trifecta". In 2010 60% of all the American calories were flour, sugar and oil. We're literally eating obesogenic rat chow and we're just maxing out all our fat cells, right? Okay, I'm almost done, I just have like two slides left. I just want to point out that your adipocytes are there for daily fat flux. Your adipocytes are supposed to expand during the day when you're eating, shrink at night when you're fasting and living off of stored fat.

And as long as you have plenty of room for fat flux you know as long as your adipocytes are empty enough that you have plenty of room for this flux, everything is fine, that's how it's supposed to work. There's also a seasonal component to this fat flux piece. All energy on Earth comes from the sun, in the summertime there's more sunlight, plants make more sugar, herbivores eat more sugar and they get fatter. Carnivores eat more fat from fatter herbivores and they get fatter.

Omnivores like humans come along - we eat more sugar and more fat and we get really fatter. The classic example is the bear, this is a classic omnivore. And in these are actual bear adipocytes in the summer. They've got sugar, they eat fruit and honey and berries. And they're also eating more fat because the animals are fatter in the summer. So they're eating more sugar and fat, they're expanding their adipocytes, they become insulin resistant and then in the wintertime everything changes.

No more glucose at all, no plant sugars at all in the wintertime. So they're just eating protein and fat. There is also less fat because animals are leaner in the wintertime. So that's really the end of my talk, but I just want to end by saying that in this country we've made it summertime, the peak of summertime, 24 hours a day, 365 days a year, just sugar and fat together day after day after day, we've all maxed out our adipocytes, half of the planet is insulin resistant and I think it's time a lot of us made it Autumn where's a lot less plant sugars and way less glucose so we can finally burn some fat for a change and for some of us it's maybe time to make it the dead of winter, where we eat no glucose at all and maybe even less fat.

So that completes my talk, yeah. Thanks.