Creon's Life Extension and Healthspan Notes and References.

See also Creon's notes on lipidology, coronary heart disease risk, statins, and coronary calcium scans

Summary of my personal situation and progress:

I am a 62-year-old (started this document when I was 55) white male living in California who was at least 30 lbs overweight¹. I went on a ketogenic diet (a.k.a. "keto") and lost over 30 lbs without exercise and without restricting alcohol. My energy levels and mental state improved too. After ~18 months of that, I went onto a program of "time restricted eating" - an intermittent fasting protocol where I only eat during the same eight-hour window every day: 12:00 noon to 8:00pm (see below). I have since kept the weight off, gained muscle, stabilized my blood glucose at optimal levels, and feel better than I ever have in my life.

Although my weight has been stable and good for years now, I have continued to lose fat and gain muscle while doing *minimal* exercise: like 15 minutes a week. (I need to make another document discussing that).

While no longer strictly keto, I eat a very-low-carb zero-sugar diet. I now eat nose-to-tail animal foods, eggs, and a few low-carb low-lectin low-oxalate vegetables with 16/8 intermittent fasting. However, I recommend the ketogenic diet for several months initially, to achieve near-optimal weight, to learn about your metabolism, and to break carb-addiction (which is the root of all evil).

In my view the essential factors to increase your health, length and quality of life are:

- 1. Maintain relatively low and stable blood glucose levels all the time (as a result you will end up eating only nutritious food). Most of this document is about achieving that.
- Eat only real foods. Don't eat processed foods. Don't eat sugar, seed oils, most carbs, lectin-containing or oxalate-containing foods. Eat only regeneratively raised foods, including at least some animal-based foods.
- 3. Get adequate amounts of high-quality sleep (1&2 will make this easier).
- 4. Increase and maintain physical strength.
- 5. Take the right supplements (you only need a few), and avoid the wrong ones.
- 6. Have lots of good times, good relationships, good sex, and meaning.
- 7. Engage in lifelong learning, including mindfulness and healthy introspection.

Of course all of the above are tied together and mutually reinforcing.

Last note of the summary section:

¹I started at BMI > 31, which is technically "obese" according to the CDC. I am now at BMI = 25.5 which is upper-end of "normal" (i.e. technically almost edging just into "overweight"), but "low risk" according to www.smartbmicalculator.com. So while I could shed another two or three pounds of visceral fat I am in far better shape than I ever was - visually and physiologically. Since I've traded a lot of fat for muscle, I think my current weight is OK.

I have recently learned that the key concept which appears to tie together all the different "interventions" (low carb, high fat, low lectin, time-restricted eating, real foods, light exposure, and more) is **mitochondrial uncoupling**. It is both a powerful concept and well-established science. For a good, well-referenced, up-to-date smart layperson's guide to mitochondrial uncoupling see Steven Gundry, MD's recent book *Unlocking the Keto Code*.

Mitochondrial uncoupling seems to be generally healthy. Here are some of the foods, supplements, and activities which are said to promote it:

Fasting, ketogenic diet, exercise, heat therapy (like sauna), cold therapy, sunlight, red light and NIR phototherapy, melatonin, caffeine, methylene blue (?), vitamin D (?)...

Basics of the ketogenic diet:

The ketogenic diet is a great way for most people to lose weight fast and - even if they are happy with their weight - to transform their health for the better without restricting calories. You can eat as much as you want, but you have to rigorously restrict *what* you eat. Or more precisely: rigorously enforce *what you do not eat*. I easily lost 35 lbs and some of my more overweight friends lost 60 to 80 lbs or more. It is not only easy, but the food you *can* eat tastes really good. It is actually not a diet - it is a lifestyle, and very enjoyable.

And while it may not work for everyone, hundreds of thousands of people and hundreds of doctors are reporting near-miraculous results (not just weight loss but reversal of type 2 diabetes, decreased blood pressure, and much more). So it is certainly worth trying.

Top level basics:

- The point of the ketogenic diet is to be in the metabolic state known as ketosis (at least for a few hours a day).
- Ketosis is the fat-burning metabolic state which evolved for times of food scarcity. This
 was common for early humans. However, in modern affluent societies food is never
 scarce, so you are never in ketosis unless you explicitly engineer it.
- When in ketosis, the body and brain get their energy from fat. When carbs and proteins are plentiful you are *not* in ketosis and the body and brain get their energy from sugar (from dietary sugars and from metabolizing carbs and proteins into sugars),
- Excess calories (there are always excess calories in our society) are stored as fat when
 not in ketosis. When you are in ketosis, excess calories are mostly turned into heat (a
 simplification).
- Fat does not make you fat. Carbs make you fat. By restricting carbs (and restricting proteins if you're young), but not restricting fat, you can enter ketosis and burn fat both dietary fat and body fat.

- To be in ketosis (without fasting) you must get at least 75% of your calories from fat every day. Until you achieve *metabolic flexibility* (the ability to quickly turn ketosis on and off, which takes a while).
- To be in ketosis (without fasting) you must <u>get no more than 10% of your calories from carbohydrates</u> each day. Until you have metabolic flexibility. Then you can add more "good carbs" back into your diet (if you want).
- The most common error people make at first is to substitute protein calories for carb
 calories. That won't work. You have to substitute fat calories for essentially all carbs, and
 substitute fat for much of your protein intake too. Once you have come close to your goal
 weight and have verified you are in ketosis at least a few hours a day, you can add more
 protein back.
- You should always avoid carbs. Particularly "bad carbs" (anything that has sugar, corn syrup, fructose, and any refined starches like most flours, rice, oats, etc. See any good book on the keto diet for extensive lists). Carbs are *not* an essential nutrient for humans (as opposed to, say, for cows where they are essential), and many carbs are basically poison. If your doctor or dietician tells you otherwise, find another one. Do your own research and you will see.
- It takes from several days to a week to get into ketosis the first time. The transition makes some people feel a little sick ("keto flu"). Once you're over it it's done if you stay in ketosis. It is important to get enough salt to avoid the keto flu, and to live a long life in general. See this video segment. Don't believe the medical/nutritional establishment's information about salt. Don't believe their information about "benefits" of a low-fat diet (they have been proven completely wrong on these topics). Don't believe pretty much anything the medical establishment has been pushing regarding nutrition for the last 45 years. Most of it has been invalidated by modern research and clinical practice.
- The other way to get into ketosis is to go on an extended fast > 3 days. I will discuss fasting later in this document.
- Rather than being about what you eat, the keto diet is more about what you don't eat. It is an elimination diet. You eliminate sugar, starch, refined carbs, and carbs in general. I also highly recommend eliminating seed oils (so-called "vegetable oils" which are made from seeds, not vegetables), lectin-containing foods (more on this at the end of the document), oxalate-containing foods, and of course highly processed food. You can identify processed food because it always comes in a package and has more than two ingredients.

If this scares you because you think fat is harmful - especially saturated fat - see this summary of evidence that fat is not harmful. If you think it is hard to find delicious satisfying food that is very-low-carb-high-fat then read on and look into ketogenic recipes. You will be pleasantly surprised.

One common question is "is the ketogenic diet the same as the Atkins diet?" Answer: No it isn't. They are similar, but not the same. The ketogenic diet has higher fat and lower lower proteinand carbohydrate-to-total calories ratios than Atkins. This means keto requires more discipline, though in some ways it is simpler.

The ketogenic diet has other names such as: VLCHF (very low carbohydrate high fat), HFLC (high fat low carb), Banting diet (historical), or "bulletproof" (a commercial trademark). There are also related diets such as Atkins, modified Atkins, modified Ketogenic, keto-carnivore, vegan keto, etc. These are subtle variations, mostly concerning the fat vs. protein caloric ratios. They are all low carb diets.

The near-miraculous benefits of carbohydrate restriction for controlling obesity and diabetes were well-known in medicine even 100 years ago and were taught to doctors and nurses. However, the medical establishment "lost the thread" about 50 years ago mostly due to political and personality forces and has been advocating for low-fat high-carb diets (the "opposite" of keto) in recent decades. This has resulted in an explosion in obesity and suffering from diabetes, metabolic syndrome, hypertension, heart disease, and most other degenerative diseases.

The "modern solution" has been to try and reverse these degenerative conditions using pharmaceuticals (drugs). This actually doesn't work for patients in the long term, though it works very well for the drug companies. It may sound controversial or even paranoid, but I suspect if you study the history of the US dietary guidelines and many of the resources linked in this document (which contain state-of-the art information from very reputable sources) you will probably agree.

Back to less controversial topics:

Very low carb diets are not just about weight loss and disease prevention. They are a lifestyle that will keep you feeling good, looking good, and healthy. Even if you are already trim and/or healthy. (look up the concept of TOFI - thin outside, fat inside).

Lowering and stabilizing blood glucose (blood sugar) is one main purpose of the ketogenic diet, of low-carb diets in general, and of intermittent fasting (see below). Low stable blood glucose is one of the most important keys for a long, healthy life. Low stable blood sugar is not only a key to losing weight, and keeping it off, but also a key to losing visceral fat (so-called "bad fat" which even some thin people have in abundance).

Low stable blood sugar also helps prevent cardiovascular disease (heart attacks, stroke, etc), other vascular diseases, diabetes (obviously), inflammation, and probably cancer, auto-immune disease, depression, and dementia (Alzheimer's). It stabilizes mood and energy levels too.

What more do you want?

Here's something more you might want: it drastically lowers your risk of serious outcomes from COVID.

What do I eat?

By popular demand, here is what I eat. This is a typical day for me. Very typical. Almost every day I eat this and only this:

time	activity	contents
08:00	"breakfast"	black coffee, and sparkling water (no, not mixed together:)
8-12	"snack"	more black coffee, more sparking water.
12:00-1:00	lunch	First food of the day. Never before 12:00 noon. Usually some fatty meat (fatty ground meat, or previous night's leftovers) or tinned seafood. Plus two poached eggs with extra yolks seasoned with salt, pepper, and sometimes other seasoning and/or sauce. All <i>ad libitum</i> but <i>never</i> anything with carbs or seed oils. Five minutes prep time. Delicious. Cheap.
1PM - 7PM	"snack"	Macadamia nuts. Or not. Maybe a small tin of smoked oysters. Or not. More sparkling water.
7PM-8PM	dinner	Fatty meat, fish, or chicken, plus optional crispy sauteed brussels sprouts, sauteed mushrooms, shallots, and/or asparagus + deglazed sauce. Seasoned creatively. Or salad w/dressing that does not contain seed oils (olive oil and avocado oil are OK). Ad libitum. No carby, high-lectin, or high-oxalate vegetables ever.
After 8PM	fasting	Nothing to eat.
alcohol	drinking	1.5 oz vodka in 8oz flavored sparkling water. Ad libitum. Occasionally a creative martini, or a spicy mezcalita sweetened with erythritol syrup. (see below)

When I'm not hungry at dinnertime I skip dinner (one meal a day, or OMAD). It took a few years on carb-restriction before this felt right. Every few weeks I skip a day of eating (which makes for a 32- to 40-hour fast). Once or twice a year I skip eating entirely for two or three days.

You will not "starve" if you do this². You evolved to be able to do this, and once you've regained your metabolic flexibility you can do it easily while maintaining consistently high energy levels.

Of course all animal foods should be sustainably - or better yet <u>regeneratively</u> - sourced. I don't know what to say if you are vegetarian / vegan, but if you are please let me know if you figure out how to make LCHF work for you.

² People say all the time "I'm starving" when they really mean "I am addicted to carbs and my blood sugar is crashing because I haven't snacked on carbs for the last two hours". The word "starving" is not only inaccurate in this case but ignorant and disrespectful of what "starving" actually means.

The basic rules are, in order of priority:

- 1) No sugar, ever. (Well, maybe once a year). This means no sucrose, raw sugar, fructose, corn syrup, HFCS, honey, agave, molasses, "cane juice", "white grape juice extract", and yes: no fruit or fruit juice³ apart from occasionally berries. Also the only lactose (a sugar) I eat is from butter or heavy cream.
- 2) Time restricted eating. Eat only in the same 8 hour window every day. I choose 12:00 8:00 pm. Some people can even do "One Meal a Day" (OMAD). I have trouble with that, but not as much trouble as I did a few years ago.
- 3) Low carb "avoid eating anything white": No sugar, flour, bread, pasta, rice, potatoes... But don't worry there are delicious substitutes for all of these (see below). Salt is fine.
- 4) High fat. Lots of olive oil, butter, avocados, almonds and mac nuts, and especially fatty meats, organ meats, and fish.
- 5) Fasting-mimicking diet or outright fasting for ≥3 days every 6 to 12 months, approximately. (see podcasts by Valter Longo linked below)

Brown rice is high-carb (and very high-lectin) so I say "no". Grains, rice, beans, cereals, pulses, legumes: no, no, and no. Don't believe me? Read until the end of this doc, especially the section about lectins.

Portions are an interesting question: High-fat low-carb does not satisfy instantly (since blood sugar does not skyrocket), but the satisfaction comes reasonably soon and lasts longer. So eating a somewhat smaller portion (remember, fat is very calorically dense) and waiting usually suffices. Getting rid of visceral body fat (the kind of fat that kills) probably requires a very-low carb *lifestyle* (not "diet") combined with intermittent fasting or fasting-mimicking diet, and maybe exercise depending on genetics.

See eg:

https://en.wikipedia.org/wiki/Adipose_tissue#Visceral_fat https://en.wikipedia.org/wiki/Non-alcoholic_fatty_liver_disease

It is becoming quite clear that visceral fat is a major predictor of mortality and many diseases of aging. This is why waist to height ratio is such a good predictor of mortality. High blood sugar and high standard deviation of blood sugar (i.e. swings in blood glucose, so-called blood glucose variability) are also excellent predictors of mortality. The LCHF diet reduces visceral fat, lowers blood glucose, and lowers blood glucose variability.

Fructose (fruit sugar) is arguably even worse for humans than sucrose ("ordinary" sugar). See: https://www.youtube.com/watch?v=L6LL92Zs5L0 and https://www.youtube.com/watch?v=ceFyF9px20Y&t=245s (longer)

³ Fructose (which is what makes sweet fruits sweet) - while "natural" - is nevertheless very bad for humans in large quantities. If you eat a lot of sweet fruit then you get way too much fructose. And if you drink fruit juice it is even worse.

Every cell is a self-repairing, self-modifying, self-sacrificing, self-replicating, self-regulating, fault-tolerant massively parallel computer / sensor network / robot / factory. Every cell.

The human body is the ultimate machine, and understanding and optimizing it is the ultimate engineering challenge.

A few key points and references.

<u>This TED talk on low carb by Peter Attia</u>, MD is quite moving. It is one of the things that started me on this journey. It may make you cry.

This <u>simple summary video by Dr. Paul Mason</u> is a good intro to low carb and why it works. And <u>this recent video of his</u> has a lot of great detail.

[I will organize and link to peer-reviewed papers on all of this soon, but you can check yourself with google scholar. Note that technically it is probably low and stable *insulin* that's really important, but insulin is hard to measure, and insulin level is driven by blood sugar level.]

Start watching <u>videos like these from Ivor Cummins</u> to have your mind blown about the terrible effects of high blood glucose on heart disease, cancer, etc., and the beneficial effects of getting your blood sugar under control. The good news is it's not hard to do.

For the most advanced, up-to-date, densest and most interesting new material I've encountered on these topics, see Paul Saladino MD's work. In particular this episode of Paul's podcast.

Ketone levels

(this section is technical and can be skipped on first reading)

When you are in ketosis, your liver produces "ketone bodies" (a.k.a. ketones) from fat and exports these ketones into the blood along with fatty acids (triglycerides) to feed all your body tissues. Fat is the alternative fuel source we evolved to utilize when food was scarce - to get us through lean times - days or weeks when the hunt goes poorly. But in the era of supermarkets, refrigeration, factory farming, restaurants, and food delivery services the hunt never goes poorly.

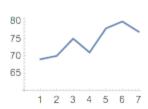
If you want to quantitatively track your ketones (and your blood sugar) there is a good inexpensive machine to get: The Abbott "precision xtra" blood glucose monitoring system. It is available for ~\$25 on Amazon. Ketone test strips for this machine cost ~\$1.50 each. Glucose test strips for it cost ~\$0.75 each. It is the best blood testing machine available to the public which I know of that monitors both blood ketones and blood glucose. It can also use "relion ultima" glucose strips which are <\$20 for 50 at Walmart or on ebay. Relion, Precision Xtra,

Freestyle Neo, and Freestyle Libre glucose test strips are interchangeable. All these machines are made by Abbott.

Recently another blood ketone/glucose test-strip monitoring machine has been announced: <u>Keto-Mojo</u>. Please contact me or comment in this document if you try it. I have not.

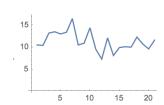
Urine test strips are also available for ketones and glucose. Based on most serious users' experience (including my own) they are not as accurate as blood test strips. But they are inexpensive, arguably less invasive, and certainly better than nothing.

I recently tested my fasting blood sugar (not ketones) with the Precision Xtra seven times in less than five minutes. The results were {69, 70, 75, 71, 78, 80, 77} mg/dL. (Median=75mg/dL, MAD=5%) Maybe I will go nuts next time and test it 20 times each on two different machines. This is just to illustrate the expected variation when using consumer blood glucose test meters.



There are now at least two breath ketone monitors available: the disposable Metron, and a non-disposable (but more expensive) Ketonix. I bought the ketonix and have been experimenting with it. It works reasonably well once you get the hang of it. No blood. No pee. But it does take about 5 minutes to warm up, and works best when plugged into a laptop so it can record your breath acetone levels into its database. It can export CSV files if you use a sql browser to parse its internal database file. Here is a video of how to export ketonix data to csv. It does not work if you've been drinking alcohol within the last hour.

I measured my breath acetone levels 21 times in 60 minutes with the Ketonix breath analyzer and got {10.6, 10.5, 13.3, 13.6, 13.1, 13.5, 16.6, 10.6, 11.0, 14.5, 9.6, 7.4, 12.2, 8.2, 10.0, 10.2, 10.1, 12.4, 10.8, 9.7, 11.7} (median=10.8 ppm, MAD=11%). I was sipping coffee (with cream+MCT oil) during this process. That could account for some of the variation. Note breath ketone (acetone) levels change much faster than blood beta-hydroxybutyrate (a.k.a. BHB, BOHB, or β OHB) levels in response to food. BHB is what the blood test strips measure.



I recommend monitoring your ketone levels with one of these methods (blood tester, urine strips, or breath monitor) to determine whether you are in ketosis or not, and at what level, and for how long each day. Your ketones will probably be highest, and your glucose lowest, just before your first calories of the day.

If you use urine sticks you are essentially limited to "none / low / high" so it is harder to track your progress and make informed decisions. But urine strips are better than nothing.

After quantitatively monitoring your ketones for several weeks you can learn to internally feel your ketone levels, and you will learn to mentally keep track of your daily fat/carb/protein caloric

intake ratios. I.e. you will learn to fairly accurately predict the readout of ketone and glucose measuring devices by monitoring your habits and your internal sensations.

Below 0.5 mmol/L ketone bodies in the blood is *not* considered "ketosis". At this level, you are far away from maximum fat-burning and other health benefits of a very-low-carbohydrate high-fat diet. However, steady fasting ketone levels from 0.2 to 0.5 are wonderful if you are at your goal weight.

Between 0.5-1.5 mmol/L is light nutritional ketosis. You'll be getting a good effect on your weight and health (particularly if you are pre-diabetic), but not optimal weight loss. If you are at this level for much or all of each day, your cells will eventually enter the state of "mitochondrial uncoupling" which is very beneficial to health.

Around 1.5 - 3 mmol/L is what's called optimal ketosis and is recommended for maximum weight loss and blood sugar control if you are diabetic of pre-diabetic.

Levels of over 3 mmol/L aren't necessary. That is, they will achieve neither better nor worse results than being at the 1.5-3 level.

Levels of over 10 mmol/L are bordering on dangerous, particularly if you simultaneously have *high* blood glucose. This condition - <u>ketoacidosis</u> - does not normally ever happen on a ketogenic diet. It can happen if you are type-1 ("juvenile") diabetic and/or alcoholic. If you have these problems consult your doctor before making dietary changes.

The middle of this lengthy and interesting blog post has good information about the differences between breath acetone levels (measured by ketonix) and blood BHB levels (measured by precision xtra and similar devices). E.g. "having high blood ketones and low levels of breath acetone appear to be a sign that you are not burning the fat you're eating." OK, but what if you have low blood ketones and high breath acetone?

Here is a blog post on the relationship of blood ketone markers to breath acetone.

Measuring blood glucose is also very important, and the precision xtra can measure both glucose and ketones.

Continuous glucose monitors (CGM).

(this section is technical and can be skipped on first reading)

I obtained a prescription for the <u>Abbott Freestyle Libre continuous blood glucose monitor</u>. It takes things to a whole new level. I may write a separate document about it someday, but for now I have added a section in it here:

Call your friendly, enlightened, supportive doctor and ask them to write you a prescription for the device (Abbott Freestyle Libre 14-day sensors), then pick it up at a pharmacy and pay out of pocket. Getting any insurance to pay for it is not worth it. Insurance requires you to be seriously sick (injecting insulin for diabetes) before they will pay for this _diagnostic_ that would have likely prevented the sickness in the first place. Welcome to the "sick care" industry.

I buy three of four sensors every time I fill the prescription. About \$70 each. They talk directly to your smart-phone.

There are youtube videos that demonstrate how to attach the sensor - which lasts 2 weeks. It talks to your phone, and to their website if you want. It makes reports like this (figure below). You will be shocked at how certain things which you may think are innocent (perhaps, say, granola and yogurt) might make glucose spike for you, which implies insulin spike which implies system-wide inflammation and damage from AGEs:

The CGM is useful for experimentation. For instance, compare a bowl of ice cream to a bowl of white rice (assuming you would eat either of those, which I would not): for some people the white rice creates a much higher glucose spike than the ice cream, and for others it is the other way around.

For me, the worst spike (glucose excursion) I ever had was from a delicious gourmet deep-dish pizza. So I am completely done with that (however keto pizza is another thing). I think I know what happened: sugars and starches in tomato sauce and cornbread crust combined with lectins in tomato sauce and gluten (a lectin) in the cornbread crust and simultaneously presented a big sugar load into my gut combined with chemicals (lectins) that drastically increase the permeability of the gut.

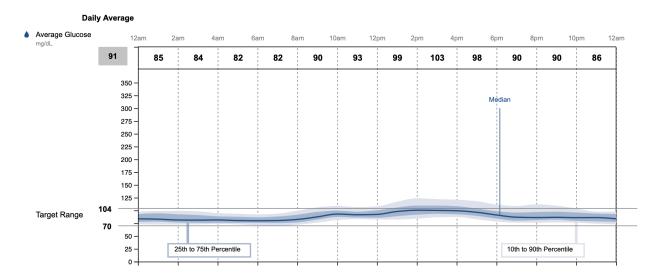
If I had been eating pizza like this several times a week for years - which I might do if I didn't know what I know from the CGM - I might be a very sick man by now.

This is what my glucose looks like these days (90-day daily pattern summary with percentiles). Rock solid fasting median value ~85mg/dL, post-prandial median ~100.

Daily Patterns

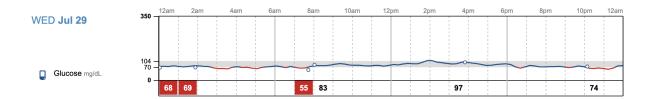
October 4, 2019 - January 1, 2020 (90 Days)



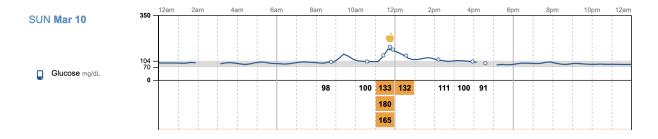


It took a while to dial this in. Basically it took a very low carb diet with intermittent fasting focused around nose-to-tail animal-based food. For me.

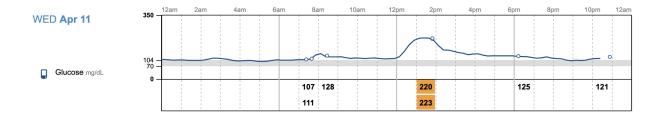
Here's a typical daily graph for me now. This low-variance, low-mean pattern is optimal for most humans AFAIK, but probably less than 5% of humans have it in the "developed" world today, which is why 75% of them are going to end up diabetic if they aren't already.



Here is a rare day where I ate some carbs for lunch (dim sum - it was worth it). I also skipped dinner:



Here is an even rarer day: I had pizza for lunch. Fancy "gourmet" pizza. It produced a very big (>220 mg/dl peak, > 5hrs long) glucose excursion. While to be honest I think this particular sensor was biased ≥10 points high, I will *not* be doing it again:



<u>Some people can avoid a glucose excursion if they eat a bowl of white rice but not not a bowl of ice cream</u>. Others, vice versa. Still others (most others I suspect) should avoid both. A CGM will help you learn a lot about your metabolism, and allow you to personalize your diet to avoid high glucose variability (which is slowly killing a *lot* of people).

Double-check with a finger stick blood test for the first two days a few times a day for every new sensor. The sensors often take a while to converge and stabilize. Note that CGM is ~15 minutes delayed compared to finger stick because CGM checks interstitial fluid (I think) and not blood.

Sometimes you will find you have a sensor which is "biased". It can read pretty consistently 10 or even 20 points high or low compared to finger stick test. And it may slowly drift ("stabilize"). However the main utility of the CGM is checking *variance* (excursions) of blood glucose, e.g. what happens in the three hours after a meal w/carbs vs. a meal without carbs.

Sometimes you can get a bad sensor that is just all over the place and never stabilizes. In that case you can call the phone number on the freestyle libre web site or the package insert and answer about 10 minutes of questions over the phone, and they will send you a new sensor for free. (they've done that for me about four times, though I no longer consider it worth my time).

Once you have worn it for a few months or at least on and off for a few months (if you are relatively healthy) you will have learned what you can tolerate - i.e. what sins you can commit and still have low, stable blood glucose. Experiment: indulge, fast for various lengths of time, go strict keto for a few weeks. Add more protein. Add more carbs. Try complex carbs but restricting simple carbs. Try fruit. Try artificial sweeteners...

Once you've learned where you can "cheat" and where you can't you can stop wearing the CGM for a while (a few months) until your lifestyle or something else changes. Occasionally check your fasting glucose w/ finger stick during that time to make sure all is good.

All of the above assumes you are not diabetic. If I were diabetic I would always wear a CGM until I had put my (T2) diabetes into remission or learned to totally control it (T1).

Glucose and ketones together

(this section is technical and can be skipped on first reading)

To convert glucose in [mg/dl] (as measured by most American consumer blood glucose meters) to [mmol/dl], divide by 18. E.g. 90 [mg/dl] = 5 [mmol/dl] (for glucose).

To compute the "glucose ketone index" (GKI):

GKI = glucose [mg/dl] / (18 * ketone [mmol/dl]) = nondimensional GKI \leq 2.0 means you have relatively high ketone levels in your blood compared to glucose. This is arguably the number to optimize (to minimize) - within reason. I.e you do not want your glucose to be too low (<<70mg/dl) or your ketones to be too high (> 8mmol/dl). You do not want to be hypoglycemic or in keto-acidosis (unlikely).

Interestingly the GKI was developed by Thomas Seyfried for treating cancer patients. His somewhat contrarian approach to cancer will blow your mind. See e.g. <u>this video</u>.

For an interesting and more complex discussion of optimum ketone + blood glucose levels, see the post <u>OPTIMAL KETONE AND BLOOD SUGAR LEVELS FOR KETOSIS by Marty Kendall</u>.

Weight loss, energy levels and general health - what to expect

Most people lose about 10 lbs within a week of eliminating carbs from their diet. First you lose water weight, then you lose glycogen weight (from the liver). Most of this will come right back if you eat a lot of carbs again.

If you stick with keto, don't drink too much alcohol, and do a little exercise (like once per week) then you should slowly lose fat weight, and replace some of it with muscle weight. In about six months of the keto diet you can drop 25 lbs (like I did) 50 lbs, or even 100+ lbs (like some of my friends - I've seen this several times). More importantly, your blood sugar will stabilize to the low end of normal. That's what you want.

You will feel great: awake and energetic throughout the day. You will fall asleep quickly and sleep soundly every night. You will not be hungry. You will not crave junk food. You will rarely if ever get sick. You will no longer get cavities or gum inflammation.

Your blood lipid profile (cholesterol, HDL, LDL, etc) may or may not move towards commonly-accepted optimal values (lipidology of ketogenic diets is very complicated. Study Peter Atia, Dave Feldman, and Ivor Cummins' work if you are interested in this). Lipidology is fascinating. I have watched hundreds of hours of lectures on it. I'm starting to gather my notes here

Warnings and Caveats

I can tell you from hard-won first-hand experience your mileage may vary. Individual genetic factors as well as age and previous lifestyle history can cause trouble with a ketogenic diet, limiting its effectiveness and in some cases (see below) making it potentially dangerous.

One problem is that for genetic reasons and/or because of "past sins" you may have lost some metabolic flexibility, making it harder to get into ketosis, harder to stay in ketosis, and easier to fall out of ketosis. For example if I am in ketosis and have, say, a glass of orange juice (a massive sugar blast - don't do it!) I will fall out of ketosis for several days. Others who have more metabolic flexibility might be back in ketosis the day after they return to the keto diet.

A potentially dangerous trap can be insufficient fiber and other micronutrients. This - possibly along with 30+ years of unhealthy lifestyle - may be what put me in the hospital in 2017 with a diagnosis of diverticulitis (a very common problem these days) - so don't do it. Make sure to eat low-carb high-fiber vegetables regularly and take necessary supplements. Avocados are an excellent high-fat high-fiber vegetable. Cruciferous vegetables are also a good way to get fiber and all-important isothiocyanates although cruciferous vegetables are not high-fat. Other vegetables are neutral (e.g. green leafy vegetables), and yet others (beets, potatoes, etc) are loaded with sugar and starch (bad).

Dietary ("nondigestable") fiber *is* digestible by the microbes in your gut, particularly in your colon. It is their normal source of food, and that is why it is essential. <u>If these otherwise</u> beneficial symbiotic bacteria do not have a source of food (fiber) they can start to digest the <u>lining of your gut</u>. Don't let that happen. That can be dangerous and even fatal if you get diverticulitis with puncture and sepsis. Eat fiber regularly. There are several types of dietary fiber, and you should consume them all from natural sources (i.e. vegetables, nuts, though arguably not seeds or grains) rather than relying on one particular type of fiber in a supplement (see 2h17m into this excellent podeast by Dr. Rhonda Patrick).

Carb-counting with vegetables and other foods can be tricky, because often the non-digestible "dietary fiber" is listed as "carbohydrate" on the label or website. But, these so-called carbs (allegedly) do not count from the point of view of a ketogenic diet.

Unlike other carbs, dietary fiber does not contribute to glycemic (blood sugar) load.

Actually, non-digestible "dietary fiber" is digestible - not by you, per se, but by microbes in your gut. If you have a healthy gut microbiome. And when those bacteria digest it, they convert much of it to fat which is absorbed by the gut.

A good brief summary of the relationship between nutrient restriction (like keto), time restriction (see below), and caloric restriction (i.e. fasting) can be found in this video from Peter Attia.

Supplements

A good brief discussion of supplements can be found here in Dr. Malcolm Kendrick's excellent (but lengthy) blog series "what causes heart disease?" or his book "The Clot Thickens". It is also worthwhile to listen to Dr. Rhonda Patrick's podcast with Dr. Bruce Ames on supplements and the "triage theory."

Here are the supplements I take every day. (the ones I no longer take are in strikethrough text). They are all based on modern biochemical research results from the top university researchers in the fields of health and nutrition. See in particular some of the podcasts listed later in this note. All taken daily at night unless otherwise noted.

4000 units of vitamin D3 (blood test revealed 5000 units was a little too much for me)

Most people who work indoors are vitamin D deficient. I was. Vitamin D supplementation is arguably the most important single modification one can make to the SAD (Standard American Diet) after eliminating sugar and probably eliminating seed oils too.

250mg nicotinic acid ("full flush" niacin, not nicotinamide)

This is to increase NAD+, sirtuins, and protein de-acetylation. Don't use the "non-flushing" kind. It is a different molecule and without the same benefits. You need to put up with the flush.

Instead of niacin now I take ResveraCell

i.e. Nicotinamide Riboside (Niagen) with Resveratrol. But I think I am going to switch to NMN + resveratrol after listening to David Sinclair.

Instead of ResveraCell I now take:

NMN (250mg/day) and Resveratrol (250mg/day). See the work by <u>Daivid Sinclair</u> for information on this protocol.

Curcumin

One 2g capsule per day. The literature looks suggestive on this. [add link]. It needs to be complexed with pepper to be absorbed but most curcumin / turmeric supplements are complexed with pepper. (note I may terminate this soon. Regular intake of "phytonutrients" is controversial.)

Vitamin K2.

K2 is important to ensure dietary calcium goes to the right places (bones, neurons, and muscle cells including cardiac muscle) but not to the wrong places (arterial plaque, kidney stones...). Almost everyone is deficient in K2. I use a <u>special blend of K vitamins</u> to reduce my coronary calcium, available from this researcher and his team.

Vitamin C

500mg. This is arguably important for collagen synthesis, which is important for many body processes. Particularly if you a have coronary calcium score >100 like me. Chromium picolinate.

Additional blood glucose control and trace mineral.

Lithium orotate

Additional trace mineral and mood stabilization.

Topical magnesium spray or magnesium glycinate capsules

Most people are magnesium deficient. Particularly problematic is a high calcium to magnesium ratio. Topical magnesium is fun - spray on the back of the knees and rub in before bed. Sleep like a baby.

Coenzyme-Q. Be

Q-sorb brand.

Metformin

Metformin is a prescription drug, not a "supplement". I take 500mg time release once per day (at night, along with all of my pills). This is what I have determined to be the minimum dose that further lowers and stabilizes my blood glucose. It is argued in many recent scientific publications that metformin is beneficial not only for diabetics and pre-diabetics, but for almost everyone, with many parallel beneficial metabolic effects (insert references). Note that it may be beneficial to cycle metformin since it may negatively impact mitochondrial (muscle) metabolism. I am now cycling metformin every few months. (see this recent paper and references therein). David Sinclaire knows a lot about this.

DHEA

25mg on the days when I take metformin.

Cal+mag+zine

Trader Joe's brand.

"Thyroid Support" supplement.

Melatonin - a few mg every night.

Zinc picolinate

50mg. Started this during the Covid-19 panic.

1000mg capsule of fish oil

Fish oil (or better: EPA+DHA+DPA or krill oil) is essential if you are on a low fat diet (which is almost certainly a bad idea). Obviously I am not on a low-fat diet. But still... 600mg capsule cod liver oil.

One packet of water-soluble Olaloa multi-micronutrient powder once a week.

This is nice if, like me, you don't like to take a lot of pills. It is available at Whole Foods Market (at least in the Bay Area).

These next few are listed here because I recently started experimenting with them several weeks after pausing metformin. Something about one of more of these next supplements appears to have made my fasting blood glucose go down quite a bit (I suspect berberine). Before taking them (and without taking metformin) my median fasting blood glucose was about

85mg/dl as measured with the CGM. After taking them the median is about 75mg/dl. Reliably. Calibrated with blood test strips and glucose test solution.

Apple cider vinegar.

I've been experimenting with this. I really enjoy a few ml of apple cider vinegar in soda water. Water with vinegar (or some electrolyte) is recognized traditionally as being very satisfying compared to plain water, and as being good for you. See Sally Fallon's AMAZING book which started me on this entire journey ~10 years ago. Recent medical literature suggests it is beneficial for blood sugar control.

Berberine

Two tablets of avmacol or brocomax (sulforaphane).

Sulforaphane is an extremely promising anti-aging and multiple disease preventing compound. Avmacol is the brand recommended by the <u>Dr Jed Fahey, who's lab has pioneered sulforaphane biochemistry.</u>

One capsule of B complex or B12

B12 and folate are very important. <u>Triage theory</u> suggests most of us are deficient. I have replaced this with this general thyroid support concection which contains B12.

inositol

Carotenoids, bioflavonoids and phytonutrients.

Eating more leafy green vegetables arguably never hurts. I have recently started taking Stephen Gundry's phytonutrient powder in water or smoothies. Approximately every other day.

White kidney bean extract.

Cissus quadrangularis extract.

Gymnema Sylverate 500 mg.

-(experiment terminated for now)

Ultra-trace mineral drops

I used to take these, but not anymore. I need to do another literature survey about their importance and efficacy. There are some plausible sounding arguments why most people in the West may be deficient in many ultra trace minerals. Basically, we no longer let flooding remineralize and re-fertilize the soil but instead practice flood control, and fertilize only with "NPK" (Nitrogen, Phosphorus, Potassium). Producing this fertilizer requires massive amounts of fossil fuel.

<u>Do not overdo supplements</u>. Particularly make sure to limit or avoid entirely iron (unless prescribed) and certain herb supplements. They can be dangerous. Vitamin E is also potentially problematic so I don't take or recommend it.

Talks (videos, playlists, and podcasts)

Here is <u>one my my youtube health playlists</u> - focused on low carb, lipidology, statins, cancer, and carnivore vs. vegetarian. Recently I have been listening to J. Stanton and Ron Rosedale. (If you want to see how deep this rabbit hole goes.) And here is <u>a playlist on meat, human health, and the environment</u> - all recent obsessions of mine.

I listen to almost all podcasts / youtube videos by these people, and read their papers when they publish:

Ivor Cummins*

Paul Saladino, MD

Peter Ballerstedt

Dr. Thomas Seyfried

Nadir Ali, MD

Aseem Malhotra, MD*

Dave Feldman*

Sioban Huggins

Peter Attia, MD

Bret Scher, MD

Dr. Paul Mason

Steve Phinney, MD

Gary Taubes

Robert Lustig, MD

Tim Noakes, MD*

Dr. Valter Longo

Dr. Guido Kromer

Dr. Rhonda Patrick

Doug McGuff

Jeff Volek, MD

Zoe Harcombe*

Linda Fettke*

Gary Fettke, MD*

Sally Fallon

Nina Tiecholtz*

Thomas Dayspring, MD

Ron Rosedale, MD.

^{*}Interestingly, these people (like me) became "COVID contrarians" long after I started following their health advice.

Books and references

The best book on the topic of fat in the diet, and how western medicine got it wrong, is "good calories, bad calories". It is exhaustive (640 pages) and well-written by Gary Taubes, one of the great science journalists. But it is for education, not for practical advice on the keto diet.

Gary Taubes also has two more recent, shorter books on the same subject which I have not read. Please post comments or reviews if you read them.

https://www.amazon.com/Why-We-Get-Fat-About/dp/0307474259 https://www.amazon.com/Case-Against-Sugar-Gary-Taubes/dp/0307701646

Other excellent books that cover this are:

- Robert Lustig, MD. The Hacking of the American Mind as well as his other books
- Ivor Cummins and Jefrey Gerber, MD. Eat Rich Live Long
- Benjamin Bikman, PhD and Jason Fung, MD. Why We get Sick

You could start with any one of them. This is actually really important. For instance we would have barely noticed COVID-19 if most people had been living this way for the last 40 years instead of the opposite way as advised by the "authorities" (CDC, NIH, AMA, etc).

As likely as not your doctors will not know about this stuff. If they don't then they need to get educated about it and/or you need to find new doctors.

For those with shorter attention spans (or perhaps with "better things to do" than prolonging your healthy years of life - I'm teasing) this TED talk by Peter Attia, MD is quite moving. It may make you cry. Also this one.

Other keto blogs, podcasts, websites:

See the "talks" section above. Most of the detailed stuff is there.

Also "fast Keto" podcast, "Diet Doctor" podcast. Carnivore Cast. Keto Girl podcast. Paul Saladino podcasts. And of course Ivor Cummins (before he got totally focused on COVID).

Podcasts (advanced):

Tim Ferriss Show guest podcasts by Rhonda Patrick, Dom D'Agostino, Peter Attia and Art DeVany. Podcasts #50, #65, #117, #172, #188, #12, #237, #228, and #239. All worth listening to.

And this...

https://hackernoon.com/biohack-your-intelligence-now-or-become-obsolete-97cdd15e395f

Ketogenic food and cooking, recipes, and ingredients

There are many keto cookbooks and pamphlets on amazon. Often poor quality. But this is a good one:

https://www.amazon.com/KetoDiet-Cookbook-Delicious-Grain-Free-Sugar-Free/dp/1592337015or"

Ivor's new book is top-quality:

The cookbook that changed everything for me when I found it accidentally 12 years ago is Nourishing Traditions by Sally Fallon. It is so much more than a recipe book. When was the last time you saw a cookbook with hundreds of literature citations and an extensive bibliography? I see she has some follow-on works out more recently which I am looking forward to investigating.

Also anyone who thinks vegetarianism (which is what veganism used to be called) is good for the planet, the body, or animal welfare should immediately read <u>The Vegetarian Myth by Lierre</u> Keith. One of the most powerful books I've ever come across (again, by accident).

Paul Saladino's new book "Carnivore Code" is one of the next things I'll read.

Extra-low-carb pasta, bread, bagels, cinnamon rolls, and cookies are available from http://www.thinslimfoods.com/. I find these are almost good as the "real thing". It's too bad Whole Foods Market and similar stores do not carry them yet. In fact Whole Foods has very few low-carb-specific processed food products as opposed to thousands of low-fat high-sugar / high-carb products. When they make the switch that will be an important milestone in health care. Unfortunately many low carb pastas and breads are high-lectin. So that doesn't work. Or they are tasteless.

One flexible, magic ingredient that is low-carb, low-lectin (and vegan, if you care) is <u>Quorn grounds</u>. Perfect for tacos, and anything where you want a ground meat substitute. Many other Quorn products unfortunately contain corn, oats and/or barley (lectins, lectins, lectins....). To be honest,

However, IMHO why bother with meat substitutes? Meat is the perfect food.

(see also this video: Dr. Michael Eades - 'Paleopathology and the Origins of the Low-carb Diet')

Whole Foods does stock <u>Lilli's chocolate (and baking chips</u>). Lilli's tastes almost as good as regular high-end chocolate, but contains no added sugar. Another very good sugar-free chocolate option, but only available for ordering for home delivery, is <u>choco-perfection</u>. I recently

tried Lakanto sugar-free chocolate which is very good. And there is monk fruit chocolate (and monk fruit sweetener) - also quite tasty and very low glycemic index.

You can make keto pancakes and waffles. Easy recipes abound on the web. Skip epicurious.com for recipes though because of their pointless anti-beef virtue signaling. They've lost their integrity. For syrup use monk fruit sweetened maple syrup (from WFM or Amazon) mixed with melted butter 50/50.

Ketogenic cocktail resources:

I like cocktails and mixology. A key ingredient for making low calorie cocktails is a substitute for simple syrup (also a substitute for agave syrup, etc). After attempting and failing several times to make a simple-syrup-equivalent using erythritol (swerve) and hot water, and after some searching and testing, I settled on Monin sugar-free liquid sweetener which is basically erythritol syrup. It is available here on amazon. It is very cheap (~\$14 for a 1 liter bottle). It has the viscosity and flavor of simple syrup, but you only need about ¼ oz to sweeten a cocktail. So I substitute it for simple syrup in the ratio ½:1. Make keto sours, margaritas, mojitos, cosmos, white Russians and craft cocktails. There are many zero-sugar flavoured syrup options to experiment with.

Another great keto cocktail ingredient is heavy (whipping) cream. Now if only someone would make erythritol-infused maraschino-cherries, and erythritol shrubs.

Creon's spicy chocolate mezcalita: In cocktail shaker combine: 2 oz. tequila or mezcal. 6-8 shakes Aztec chocolate bitters. 2 squirts habeñero bitters. ¼ oz. monin (erythritol) syrup. ½ oz. or more lime juice. Add a lot of ice. Shake vigorously. Strain.

Summary of science and clinical data

I need to add the recent trials of VLCHF and T2DM here. There are fantastic new results from several studies and meta-analyses.

From Dietary Carbohydrates Impair Healthspan and Promote Mortality

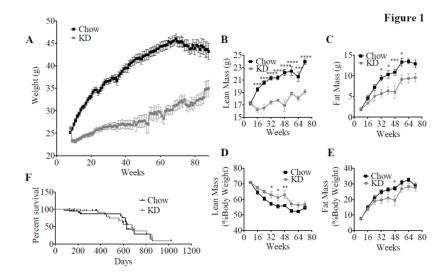
"In the PURE study [>135,000 participants from 18 countries], most notably, the almost complete removal of carbohydrates (<1%) from the diet to generate a ketogenic diet extended lifespan compared to a high-carb diet. However, reconstituting only 10% of energy of the ketogenic diet by sugar abolished this effect (Roberts et al., 2017), suggesting that specifically sugar (rather than carbohydrates in general) has the most relevant effect on lifespan....re-analysis additionally adjusting for household income and wealth, as well as for socioeconomic status of the respective country, did not affect the key observations of the study by any means"

Long term studies on effects of ketogenic diet

Anecdotal evidence of the health benefits of VLCH diets are well-known (Eskimos, etc). However this is confounded by studies that show some long-term problems such as obesity, decreased glucose tolerance and fatty liver when genetically modified mice (ob/ob, NZO, and even MRL strains) with are fed a ketogenic diet (KD).

However, very few controlled studies of the lifelong effects of KD in normal mice (or other mammals) are available, I found this one: <u>Adaptive changes in amino acid metabolism permit normal longevity in mice consuming a low-carbohydrate ketogenic diet</u>. Here is the abstract, emphasis added

Ingestion of very low-carbohydrate ketogenic diets (KD) is associated with weight loss, lowering of glucose and insulin levels and improved systemic insulin sensitivity. However, the beneficial effects of long-term feeding have been the subject of debate. We therefore studied the effects of lifelong consumption of this diet in mice. Complete metabolic analyses were performed after 8 and 80 weeks on the diet. In addition we performed a serum metabolomic analysis and examined hepatic gene expression. Lifelong consumption of KD had no effect on morbidity or mortality (KD vs. Chow, 676 vs. 630 days) despite hepatic steatosis and inflammation in KD mice. The KD fed mice lost weight initially as previously reported (Kennnedy et al., 2007) and remained lighter and had less fat mass; KD consuming mice had higher levels of energy expenditure, improved glucose homeostasis and higher circulating levels of β-hydroxybutyrate and triglycerides than chow-fed controls. Hepatic expression of the critical metabolic regulators including fibroblast growth factor 21 were also higher in KD-fed mice while expression levels of lipogenic enzymes such as stearoyl-CoA desaturase-1 was reduced. Metabolomic analysis revealed compensatory changes in amino acid metabolism, primarily involving down-regulation of catabolic processes, demonstrating that mice eating KD can shift amino acid metabolism to conserve amino acid levels. Long-term KD feeding caused profound and persistent metabolic changes, the majority of which are seen as health promoting, and had no adverse effects on survival in mice.



See also: http://www.scielo.br/scielo.php?pid=S2359-39972016000400405&script=sci arttext

But this is not the whole story since the "high fat" chows that rats consume in many keto studies are loaded with seed oils (a.k.a. vegetable oils), which are toxic. Sometimes they also contain sugar. If anyone knows of a *real* ketogenic RCT on mice or other animals which examines overall morbidity and mortality, please let me know.

Ketogenic Diet, Triglycerides, Cholesterol, and all that.

A huge topic. Just some notes here.

One problem with the keto diet is what it does to the average person's lipid panel. Of course it raises triglycerides. It also seems to raise LDL-C (insert references). But this is complex because increased trigs and LDL-C does not necessarily cause CVD. Increased LDL-P and particularly increased APO-B seems associated with CHD. However, even if the keto diet increases APO-B (and I do not know whether it does or not) the subsidiary benefits may outweigh whatever cholesterol-related risks there are. This is very complicated and the subject of intense research. See the five hours of material by Thomas Dayspring on Peter Attia's podcast.

Also see <u>The Straight Dope on Cholesterol</u> - a nine part blog by Peter Attia. And watch or listen to everything you can by Ivor Cummins.

And finally, for the story I currently have the most belief in, read Dr. Malcolm Kendrick's excellent (but lengthy) blog series "what causes heart disease?" or his book "The Clot Thickens".

Metabolic flexibility articles which I found enlightening:

http://www.gnolls.org/1984/the-science-behind-the-low-carb-flu-and-how-to-regain-your-metabolic-flexibility/

selected scholarly articles on ketogenic diets (this is what got me started, but it is somewhat dated. If you are interested in a curated list of relevant scientific papers ask me in the comments):

The basics of ketone metabolism.

http://www.nature.com/eicn/journal/v67/n8/abs/eicn2013116a.html

http://www.tandfonline.com/doi/abs/10.1080/14017430802014838?journalCode=icdv20

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4405421/

http://drhyman.com/blog/2016/05/05/fatty-liver-is-more-dangerous-than-you-might-realize-heres-how-to-heal-it/

http://www.biomedcentral.com/content/pdf/1743-7075-5-36.pdf

http://www.biomedcentral.com/content/pdf/1743-7075-2-34.pd

https://www.researchgate.net/profile/Sami_Asfar/publication/225278771_Effect_of_low-calorie_versu

s low-carbohydrate ketogenic diet in type 2 diabetes/links/00b4951cbf8b100350000000.pdf

http://online.liebertpub.com/doi/abs/10.1089/154041903322716723?journalCode=met

http://www.nutritionjrnl.com/article/S0899-9007(09)00177-4/fulltext?mobileUi=0

http://link.springer.com/article/10.1007/s11010-007-9448-z

http://jcn.sagepub.com/content/early/2013/05/14/0883073813487596.abstract

http://www.sciencedirect.com/science/article/pii/S0940299310000862

http://diabetes.diabetesjournals.org/content/27/11/1087.short

http://www.biomedcentral.com/content/pdf/1743-7075-5-14.pdf

http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0018604

https://www.researchgate.net/profile/Pamela_Dyson2/publication/23226271_A_review_of_low_and_reduced_carbohydrate_diets_and_weight_loss_in_type_2_diabetes/links/02bfe512df087c071100000

http://ajpendo.physiology.org/content/292/6/E1724.short

https://www.researchgate.net/profile/Sami_Asfar/publication/9051371_Ketogenic_diet_modifies_the_risk_factors_of_heart_disease_in_obese_patients/links/02bfe5111cffe22508000000.pdf

http://www.nutritionandmetabolism.com/content/2/1/16

http://onlinelibrary.wiley.com/doi/10.1111/j.1464-5491.2005.01594.x/abstract?userlsAuthenticated=false&deniedAccessCustomisedMessage=

http://www.ijcasereportsandimages.com/archive/2014/010-2014-ijcri/CR-10435-10-2014-clemens/ijcri-1043510201435-toth-full-text.php

http://www.sciencedirect.com/science/article/pii/S0899900714003323

http://www.mdpi.com/1660-4601/11/2/2092/htm

http://www.zaggini.com/media/a-review-of-low-carbohydrate-ketogenic-diets 30.pdf

http://pediatrics.aappublications.org/content/101/1/61.short

http://gimed.oxfordiournals.org/content/100/10/659

http://www.nutritionj.com/content/7/1/30

http://ajcn.nutrition.org/content/85/1/238.short

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2716748/

http://www.sciencedirect.com/science/article/pii/S1871403X07000816

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4737348/

Other interesting links:

https://www.ketovangelist.com/seven-books-that-you-absolutely-must-read/ (confirmation) http://www.ketogenic-diet-resource.com/metabolic-pathways.html

Metabolism paper links:

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4414487/

http://www.cell.com/trends/endocrinology-metabolism/fulltext/S1043-2760(13)00156-2

http://www.sciencedirect.com/science/article/pii/S1550413116306556

Weight loss notes

- 1) Weight fluctuates. You are lightest in the morning.
- 2) Most of the real weight (from fat) that you lose is exhaled as CO2 during the night. The rest is fluctuation that does not correspond to fat loss.
- 3) The amount of salt you eat the night before makes a big difference in temporary weight due to water retention. Restaurants use a lot of salt, so it is almost inevitable that if you eat dinner out then the next morning you will be a couple of pounds "heavier". That's just temporary water retention.
- 4) Poop & pee can make you fluctuate ± 0.5lb or so.
- 5) Female hormonal cycle causes fluctuation of ±1.5% of body weight (approx).

- 6) Consumer-grade digital bathroom scales, even if they are new and undamaged, can differ by ±2% from one another. Use a single scale and track delta and delta%.
- 7) Consider getting a DXA scan when you start, and then again after diet/exercise/lifestyle changes have been in place a few months. DXA will tell you fat/muscle/bone (and bone density) percentages in every major area of your body. This is important. For most men and many women who aren't grossly obese, as you approach middle age, health-span is increased not so much by *losing* weight as by *shifting* body weight from visceral adipose tissue ("belly fat"), liver fat, and muscle fat to: lean mass (actual muscle) and subcutaneous ("brown") fat, and to denser bones. DXA scans will let you monitor this progress precisely. A DXA scan from bodyspec.com is ~\$50 and takes ~15min. Non-invasive. They have several trucks that go around major cities for this, but you have to schedule in advance.

Best recipes for keto meals and snacks.

Keto Waffles (google)

Pancakes (google)

Low-carb bagels. Toast and spread with butter then avocado. Add salt and pepper.

See this nice blog: https://www.ketogenic-diet-resource.com/low-carb-recipes.html

Discussion of Swerve / erythritol and keto desserts.

Papers on sugar alcohols. (TBA)

Note: you can substitute erythritol (a.k.a. "Swerve", available at Whole Foods Market) 1:1 or 0.5:1 for granulated sugar. It bakes, dissolves, and cook the same. IMHO it is better than stevia in every way

Rhonda Patrick's low carb lemon tart recipe.

Add: keto Choc. chip cookies recipe.

Keto restaurants and keto-friendly menu selections from particular restaurants

In San Francisco:

<u>Sparrow</u> on Haight St. between Clayton and Cole

Foundation Cafe on Kearny between Pine and Bush

General:

https://www.ruled.me/keto-and-fast-food-on-the-go/

http://ketointhecity.com/blog/2016/5/29/eating-out-on-keto-my-top-10

Butter coffee rant

<need to write this section>

Miscellaneous

Hormone dependent lipase

Dawn Phenomenon

http://www.diabetes-book.com/?s=the+truth+about+fats

http://www.diabetes-book.com/incretins-low-carb-high-fat-diet-and-diabetes/ (Incretin mimetics)

Advanced Topics

The next big things: beyond keto - metformin, nicotine, stresses, extreme isometrics, heat shock proteins, sulforaphane(?), autophagy, caloric restriction, fasting, intermittent fasting, time-restricted feeding, refeeding, fasting mimicking diets, the carnivore diet, and the controversial role of lectins in inflammation and metabolic syndrome.

time-restricted feeding, one-meal-a-day, and fasting.

Please listen to some of the podcasts listed below for details.

The most effective kind of time-restricted feeding (TRF), or time restricted eating (TRE) seems to be "early time restricted feeding" (eTRF) where you eat only during the eight hours after waking every day. I.e. eat only from 8AM to 4PM. Insulin sensitivity is highest early in the day, so that's the preferred time to eat for optimum health. The idea is to fast for 16 hours a day (including sleep). I eat only between 12 noon and 8pm because it's easier socially. I've been doing it for a few years and I feel great. See https://www.selfhacked.com/blog/intermittent-fasting/

Another, likely even more beneficial alternative is "OMAD" - one meal a day. I tried it but it is harder than 16/8, and I am doing fine with 16/8 AFAICT. Instead of OMAD I do two or three day water-only fasts a few times per year.

For all of these, snacks *are* considered meals. Alcohol may or may not be considered eating. Black coffee and plain tea are not considered eating by most researchers / practitioners although as of late 2017 the detailed metabolic consequences of coffee and tea consumption

during fasting are not understood. However, modern research suggests coffee (even de-caffeinated) and even nicotine (but *not* smoking) are beneficial. As they say, "more research is needed".

Anyone who follows the last few years of research in these areas is doing some form of time-restricted eating, or something that requires more discipline like 5/2 intermittent fasting (five days eat / two days fast per week), or fasting mimicking diets (super low calorie high fat diet for five days in a row a few times a year), or actual 4 to 5 day fast twice a year. The latter are obviously harder, but are probably even more beneficial. The theoretical, biochemical, animal, and human data are compelling for all of these, and it appears that many if not all of the benefits of draconian caloric restriction can be obtained by methods which are far less draconian, easier, and more pleasurable.

One meal a day (OMAD)

This is a long term strategy for weight (fat) loss, glucose control, autophagy (see below) and general health. It is exactly what it sounds like. Top researchers at top universities studying longevity and nutrition practice OMAD. Presumably they know something. The basics of OMAD is to eat only one meal each day. The same meal each day (e.g. dinner) - just pick one. For weight loss construct the meal so that you are at a slight daily calorie deficit. *Not* a massive daily calorie deficit (for many reasons). The calories should come approximately 50% from fat, 40% from protein, and 10% from carbs. People practice OMAD for years to good effect.

Autophagy

The key point is to use fasting, and/or time-restricted eating, and/or OMAD, and/or a very strict ketogenic diet to regularly cycle in and out of a state of <u>autophagy</u> where damaged proteins and damaged cells are recycled. Then, importantly, after a fast of sufficient duration to induce autophagy is broken (during refeeding), stem cells re-differentiate creating new replacement cells. These new cells have long telomeres and fresh (i.e. error-free, unoxidized, correctly folded) molecules. [note: the Nobel prize in medicine was awarded in 2016 for the discovery of the mechanisms of autophagy].

Here is one of the only connections I have run across connecting keto and autophagy. It comes from Dr. Jason Fung in this video. The connection is that autophagy is controlled by MTOR (mammalian target of rapamycin), and MTOR is a *protein* sensor, not a general food or calorie sensor. So, if you eat a diet consisting [almost] completely of fat, then the protein sensor MTOR will indicate very low protein and autophagy will be triggered. Further, it appears that *branched chain amino acids* (subcomponents of many but not all proteins) are the real culprit. (insert references).

I believe this is how it works: all proteins are built from amino acids, and our bodies cannot synthesize any of the 20 essential amino acids. (They are "essential" in the human diet). We normally ingest amino acids only by ingesting protein. Hence, if we stop ingesting protein then the *only other source* for essential amino acids is from catabolism (breaking down) of existing

protein in our body - i.e. in our cells. Autophagy is the first tier of this process (before abject starvation, i.e. wasting). To avoid wasting and starvation on an protein-deficient diet, the body uses autophagy to preferentially recycle "garbage" proteins: those proteins which are damaged - oxidized, misfolded, inappropriately glycated, inappropriately methylated, etc. Autophagy brought on by fasting recycles damaged molecules, organelles, and even whole cells. Then, subsequent re-feeding initiates proliferation of new (and hence undamaged) cells from stem cells.

Important Links on fasting, intermittent feeding, autophagy, etc.

https://www.sciencedaily.com/releases/2017/01/170106113820.htm

Dr. Rhonda Patrick interviews Dr. Satchin Panda on circadian rhythms and time restricted feeding:

https://www.youtube.com/watch?v=-R-eqJDQ2nU https://www.youtube.com/watch?v=iywhaz5z0qs

Dr. Rhonda Patrick interviews Dr. Valter Longo on fasting mimicking diets https://www.youtube.com/watch?v=d6PyyatqJSE

Dr. Rhonda Patrick interviews Dr. Guido Kroemer on Autophagy, Caloric Restriction Mimetics, Fasting & Protein Acetylation

https://www.youtube.com/watch?v=Gm626Mgpvel

Dr. Rhonda Patrick interviews Dr. Ronald Krauss on LDL Cholesterol, Particle Size, Heart Disease & Atherogenic Dyslipidemia https://www.youtube.com/watch?v=7qZt9DQqtZl

Additional good links on fasting:

https://idmprogram.com/fasting-physiology-part-ii/ https://idmprogram.com/fasting-and-growth-hormone-physiology-part-3/

Lectins.

This section should probably be a whole document of its own. It is more controversial and less accepted than ketogenic diets and fasting. However, if you suffer from leaky gut, IBS, allergies, autoimmune disease, inflammation, gluten sensitivity, arthritis, or CHD, you might be well-advised to give a *low-lectin diet* a try.

Lectins (carbohydrate-binding proteins) are ubiquitous throughout biology. Some lectins are essential for human life, and some lectins are used by bacteria and other pathogens to gain access to their host organisms. Many lectins are synthesized by plants, particularly nightshades (tomatoes, eggplant), grains, squashes, cucumbers, legumes, beans, and some nuts. Plants produce lectins for many reasons, but one important reason is to poison, weaken, and sicken animals that eat their seeds and other tissues. This is not disputable: your doctor might not know it but botanists and veterinarians have known it for decades.

Gluten is a plant lectin, but it is far from the most toxic: The lectins from a few raw or undercooked kidney beans can put you in the hospital. And ricin (a lectin and biowarfare agent) from a few castor beans can put you in the morgue. It only takes about 10mg of ricin to kill someone.

Steven Gundry MD is the main proponent of the low-lectin diet. Wikipedia has a self-contradictory and rather ad-hominem section on Stephen Gundry.

For the full court-press, not very technical but apparently working for a lot of people, see Gundry's books:

The Plant Paradox: The Hidden Dangers in "Healthy" Foods That Cause Disease and Weight Gain (I read this four years ago and my wife and have followed a low-lectin diet ever since. It has *really* helped her, and definitely improved my gut health if nothing else.)

The Plant Paradox Cookbook: 100 Delicious Recipes to Help You Lose Weight, Heal Your Gut, and Live Lectin-Free

<u>The Longevity Paradox: How to Die Young at a Ripe Old Age</u> (Gundry's latest book. I would like to read it.)

While I appreciate Stephen Gundry, I still think some of his claims are suspect - particularly his insistence on the benefits of only eating very small amounts of animal-based foods. One has to wonder, given that much of his life and career was at Loma Linda University, what influence the 7th day adventist vegetarian religious nonsense has on him. To be fair, he did interview at least one proponent of the carnivore diet on his rather interesting podcast, and he did so from a balanced, open point of view.

I appreciate Stephen Gundry but I question some of his claims and his commerciality. But he's helped me, my family, and apparently a lot of other people.

For another voice discussing the issues with lectins in the human diet, and if you prefer videos over books, see this talk by Paul Mason, MD.

I've dug deeper, and here are some notes on Lectins I cribbed from several academic books and surveys:

From: LECTINS Second Edition, by NATHAN SHARON and HALINA LIS. Department of Biological Chemistry, Weizmann Institute of Science (Springer, 2004):

"This is the second edition of our little red book *Lectins* published in 1989. In the intervening years well over 10,000 articles have appeared with lectins as the main subject, and more than twice as many in which they were touched upon, as well as around 20 books." (preface)

"The toxicity for animals of certain plant lectins has been recognized since the earliest days of lectin research" (p27).

"Ricin is one of the deadliest poisons known; it is by weight about ten times as poisonous as cobra venom...Ricin, as well as the related plant toxins abrin, modeccin, volkensin and viscumin, are the only toxic lectins for which the mechanism of action has been investigated in detail...a single molecule of ricin can inactivate ~2000 ribosomes which explains why these substances are so toxic: one (or a few) molecule(s) that enters a cell is sufficient to cause its death" (pp.313-314)

"Certain plant lectins are toxic for insects and higher animals, and several of them are inhibitors of fungal growth. It has therefore been assumed that these proteins function in the defense of plants against predatory animals and different kinds of phytopathogens" (p339)

"When ingested by experimental animals, PHA bound to the brush border cells of the intestine, where it was rapidly endocytosed. Upon entering the cells, the lectin enhanced their metabolic activity leading to hyperplasia and hypertrophy of the small intestine. Moreover, ingestion of PHA or raw beans by experimental animals caused acute nausea followed by vomiting and diarrhea. The discomfort was so severe that the animals were reluctant to consume a diet containing PHA, and in some instances they rather starved." (p340)

"A potential role for lectins in the defense of plants against insect attack was recognized more than 20 years ago" (p341)

"The possibility of controlling plant pests by using suitable insecticidal lectins in transgenic crops is receiving serious attention, but is still at the experimental stage." (p342)

From: "Lectins as Plant Defense Proteins" Willy J.Peumans and Eisj. M. Van Damme. Laboratory for Phytopathology and Plant Protection, Katholieke Universiteit Leuven, Leuven, Belgium Plant Physiol. (1995) 109: 347-352:

"A breakthrough occurred when it was understood that most plant lectins may not only play a role in the plant itself, for instance, as a store of nitrogen or as a specific recognition factor, but also

interact with glycoconjugates of other organisms. They interfere with the normal functioning of that organism."

"lectins can be interpreted as an indication of the plant's successful development of recognition/reaction molecules against different types of sugar-containing receptors."

"Although the whole plant is exposed to a continuous threat of pests and diseases, some tissues or organs need extra protection, since they play a key role in the survival of the individual or the species... For instance, seeds ...one can reasonably argue that they have developed (passive) defense systems to protect their storage organs and seeds."

"one can predict that these proteins protect plants against animal predators. Fortunately, the toxicity of lectins toward higher animals is well documented because of studies assessing the possible health risk of lectins present in plants used in food and feed production."

"Since the cells at the luminal site of the digestive tract are covered with membrane glyco-proteins and highly glycosylated mucins, there are countless targets for interactions with dietary plant lectins."

"When the lectin enters the cells, it induces an enhanced metabolic activity that eventually leads to hyperplasia and hypertrophy of the small intestine"

"Although most of the research on toxic lectins has been done with PHA, there is plenty of evidence that other lectins provoke similar effects"

"Several other lectins from seeds and vegetative storage organs bind to the intestinal mucosa of rats and thus disturb the normal function of the intestine. In addition, some cause systemic effects such as an enlargement of the pancreas (Pusztai et al., 1993). These lectins may also play a role in the defense against predators. The presence of moderately toxic proteins in seeds and vegetative storage organs may be an evolutionary adaptation. Although the presence of toxic lectins may not completely protect a seed or plant part from consumption, the reaction of avoidance by the animal may be beneficial for the survival of the [plant] species."

From: "Plant Lectins". Willy J.Peumans and Eisj. M. Van Damme. Department of Molecular Biotechnology, Laboratory of Biochemistry and Glycobiology, Ghent University, Gent, Belgium. Advances in Botanical Research, Vol. 48 Incorporating Advances in Plant Pathology. (2008):

"Some legumes accumulate up to 10% lectin (on a total protein basis) in their seeds."

"Most classical [plant] lectins can be considered storage/defense-related proteins"

"These plant lectins are not involved in specific recognition phenomena in the plant cell itself but are a special class of aspecific constitutively expressed defense proteins that help the plant to cope with attacks by predators, such as phytophagous invertebrates and/or herbivorous animals."

From: "Plant lectins: Occurrence, biochemistry, functions and applications". Harold Rüdiger and Hans-J. Gabius. Glycoconjugate Journal 18, 589–613, (2001):

"A well-studied example of the first group is given by the lectin fraction from the common or French bean, Phaseolus vulgaris... Infamous as toxic ingredients of insufficiently cooked beans, this lectin fraction can cause mal-adsorption and irritations in the digestive tract."

From: https://en.wikipedia.org/wiki/Phytohaemagglutinin:

"Phytohaemagglutinin (PHA) is a lectin found in plants, especially certain legumes....It is found in the highest concentrations in uncooked red kidney beans and white kidney beans (also known as cannellini), and it is also found in lower quantities in many other types of green beans and other common beans (Phaseolus vulgaris), as well as broad beans (Vicia faba) such as fava beans...As a toxin, it can cause poisoning in monogastric animals, such as humans,"

From: "Lectins, Agglutinins, and Their Roles in Autoimmune Reactivities". Aristo Vojdani, PhD, MSc, CLS. ALTERNATIVE THERAPIES IN HEALTH AND MEDICINE A PEER-REVIEWED JOURNAL • VOL. 21, SUPPL. 1:

"Approximately 30% of our food contains lectins, some of which may be resistant enough to digestion to enter the circulation. Because of their binding properties, lectins can cause nutrient deficiencies, disrupt digestion, and cause severe intestinal damage when consumed in excess by an individual with dysfunctional enzymes. These effects are followed by disruption of intestinal barrier integrity, which is the gateway to various autoimmunities. Shared amino acid motifs between dietary lectins, exogenous peptides, and various body tissues may lead to cross-reactivity, resulting in the production of antibodies against lectin and bacterial antigens, followed by autoimmunity."

"This autoimmune reactivity depends on the interaction of the dietary lectins with the gut microbiota and the facilitation of bacterial growth, such as Escherichia coli and other enterobacters. Release of bacterial toxins, such as lipopolysaccharides, increases the permeability of the gut, allowing increased passage of dietary lectins, other food antigens, and bacterial toxins to the periphery. The entry of dietary lectins, proteins, and bacterial toxins into the circulation can result in the binding of various lectins to almost every single target-tissue antigen..."

"dietary lectins interact with enterocytes and lymphocytes, which may facilitate the translocation of both dietary and gut- derived pathogenic antigens to peripheral tissues, which in turn causes persistent, peripheral, antigenic stimulation. This stimulation and immune response against mimicking peptides can cause antibodies or T lymphocytes to cross-react with both foreign and endogenous peptides. That cross-reaction thereby breaks immunological tolerance, causing more IgM or IgA antibodies to be produced against IgG-bound lectins; the resultant autoantibodies are called rheumatoid factor. It has been proposed that eliminating dietary elements, particularly lectins, and other cross-reactive foods that adversely influence both enterocyte and lymphocyte structure and function can reduce the peripheral antigenic stimulus and, thereby, result in a diminution of disease symptoms in certain patients with RA [rheumatoid arthritis]"

"It is proposed that the elimination of certain dietary elements, including lectins, that adversely influence both enterocyte and lymphocyte structure and function can reduce the peripheral antigenic stimulus and, thereby, result in a diminution of disease symptoms in some, but not all,

patients with autoimmune disorders. Therefore, if individuals have an autoimmune condition, they owe it to themselves to explore the link between lectins and autoimmunity in their journeys toward health and recovery"

From: "Cereal Grains: Humanity's Double-Edged Sword". Loren Cordain. Simopoulos AP (ed): Evolutionary Aspects of Nutrition and Health. Diet, Exercise, Genetics and Chronic Disease. World Rev Nutr Diet. Basel, Karger, vol 84, pp 19–73 (1999):

"Of the eight commonly consumed cereal grains, lectin activity has been demonstrated in wheat, rye, barley, oats, corn [206], and rice [207] but not in sorghum or millet [208]. The biological activity of lectins found in cereal grains are similar because they are closely related to one another both structurally and immunologically [209]. The best studied of the cereal grain lectins is wheat germ agglutinin (WGA), and the in vitro biological effects of WGA upon tissues and organs are astonishingly widespread. Virtually every cell in the body, and every extracellular substance can be bound by WGA"

"dietary lectins represent powerful oral immunogens capable of eliciting specific and high antibody responses [213]."

"Numerous studies have demonstrated that feeding of wheat gluten to rats or mice, which are genetically predisposed to IDDM, increases the expression of the disease [255, 271, 272]. It remains elusive how wheat proteins increase the expression of IDDM in genetically predisposed animals."

From: "Toxic proteins in plants" Liuyi Dang, Els J.M. Van Damme. Ghent University, Dept. Molecular Biotechnology, Laboratory Biochemistry and Glycobiology, Phytochemistry 117, 51–64 (2015):

"The wide distribution of lectins, also in edible plants and crops, makes the potential toxicity of these proteins an important issue for health of both humans and animals. The toxicity of lectins to animals can vary greatly, ranging from merely antinutritional properties to lethal effects."

"Lectins present in food can interact with the epithelial surface of the intestines and can induce physiological effects in humans and other animals. Although some lectins have a beneficial effect, several lectins - mainly legume lectins - have a detrimental effect.

From: "EFFECTS OF PLANT LECTINS ON HUMAN ERYTHROCYTE AGGLUTINATION" Nadja Zubcevic, at al. Department of Biology, Faculty of Science and Mathematics, University of Sarajevo (2015):

"Plant lectins are carbohydrate binding proteins or phytohaemagglutinins present in most plants, especially seeds and tubers, which include cereals, potatoes and beans. Lectins have great significance in the diet because of their involvement in gastrointestinal difficulties and erythrocyte agglutination."

"Lectins bind to glycosyl groups on the membranes of cells lining the digestive tract; this lectin binding is used as a potential tool for the specific targeting of drugs and for bioadhesive

applications. Areas of epithelial cells and even whole zones are necrotized, which can be observed in biopsies of the mammal (14) and insect (15) intestines...many other responses have been noted including mutagenesis (16), formation of vacuoles (17) and inhibition of exocytosis."

"Over the past few decades, it has been reported that many lectins are toxic and inflammatory. Lectins are resistant to both heat and digestion. Some lectins are highly resistant to gastric acid and proteolytic enzymes (18). According to some studies, some foods containing lectins pass through the intestinal wall, which can result in the deposition of lectins in distant organs (19)."