Hey everyone, Thanks for all the questions about coffee - since there was a lot of them and I want to try and give good answers, I've split it up into two parts so if you don't see your question now it will show up in the next post.

Coffee, Insulin & Coffee while Fasting

Ali Fajar Indrawan

"Hi! I am interested in how coffee and insulin are interelated. While studying about intermittent fasting, some opinions states that we should not have too much coffee since it triggers insulin in our bodies."

Renato Molina

Influence of coffee in ketosis

John Solano

I heard drinking coffee gives you a better chance entering ketosis. I wonder if that claim has merit.

Re: John & Renato, Coffee (caffeine) promote ketosis
This is addressed a little in the butter coffee video and in the extended transcript (also attached to this post for reference), but: Coffee increases plasma glucose, FFA and slightly increases insulin. [R,R2] However, it also increases ketone production. [R° & link to full text] So, I wouldn't be worried about being kicked out of ketosis and losing the ketotic benefits of IF when you drink coffee. But there's a bit more to say about this - see Rigo Tamas's question

(Mark Sisson has a decent post on coffee and insulin.)

Rigó Tamás

What about black coffee and plain tea while fasting? I'm talking about extended fasts, eg.: more than 2 days. Does it inhibit autophagy from taking place or does it actually aid autophagy?

This is a really interesting question that I was wondering about myself. That is, coffee promotes ketone production in people who are not in ketosis, as per the study titled "Caffeine intake increases plasma ketones: an acute

metabolic study in humans." [R^c]. However, does coffee give you even more ketone production if you're already in a highly ketotic state? And I think this is what Renato Molina and John Solano may have been referring to. I haven't been able to find data on this, but I did a 7 day fast with my brother several months back when he visited Japan, and we both agreed we just kinda felt like crap most of the time. (Favorite line from my brother: "It's already day 5, Where's our goddamn superpowers?") Maybe we should have been moving around more or something - we played a lot of Fallout 4... but we were also drinking coffee and we were both suspicious of it. We stopped the coffee on day 5, but we didn't feel particularly different after stopping. I've felt much better on other fasts, perhaps the case with this one was that we were eating pretty crappily before starting the fast? (We were trying out a bunch of Tokyo restaurants). I just got a blood glucose monitor which can check for ketones, so when I do another extended fast, I'll make sure to test my ketones while fasting, then after they get guite high I'll drink some coffee and see what happens. As for autophagy, Coffee actually promotes autophagy! This is according to a study[R] done by Dr. Guido Kroemer & colleagues - he appears as a guest on Dr. Rhonda Patrick's show (link should take you to the section where he discusses coffee and autophagy). However, the same question applies: if your physiology is already promoting plenty of autophagy, would coffee take it even further or reduce it?

Coffee vs. Tea & Different coffees & Different preparation methods Tristan Walker

How do the effects of coffee for you compare to those of green tea or yerba mate or similar drinks? Do you find that the quality or variety of coffee you drink changes the way it affects you?

Good question - I get less of a buzz from teas (I've had plenty of green tea and had yerba mate once or twice), which is unsurprising as there's less caffeine. I like Jasmine tea at times because it has L-theanine and not too much caffeine, so I get a nice gentle wakefulness.[R] (Ironically I let the Jasmine tea I'm having now steep too long and it's giving me a bit of jitteriness.)

Starbucks coffee tastes burnt, so I usually avoided that and drank cheap coffees (like this from Family Mart). Those made me feel anxious and a bit nauseous/dehydrated, especially if I had it black. I saw the Dave Asprey thing about mold in coffee and why we should buy his coffee, so before investing in his product I just tried some organic coffee. Thanks to the organic, I could enjoy coffee without feeling crappy. I've had this, this and this and the Asprey coffee. Felt good on all of them, didn't feel particularly different on the Dave Asprey coffee.

Jorg Janke

Coffee has quite a bit of a price range ... from a biochemistry perspective is there a difference? If yes, what are the things to look for?

Excellent question. Yes, different coffees most likely have different biochemical effects as they will have different compounds depending on the coffee variety, roasting and processing. [R*]



"An overview of metabolism of the key components of coffee identified critical metabolic steps regulating the final concentration of metabolites that determine coffee quality. Coffee metabolism is influenced by both G and E (genotype and environment) and explains the higher quality of Arabica when compared to Robusta as well as the improvement of coffee quality by shade." As for the "If yes, what are the things to look for?" part of your question, if you really want to dig into the compounds in coffee, you might

find some specifics in this study, but more practical things to look for are:

As for what to buy:

-Robusta: More caffeine | Arabica: Less caffeine

-Light Roast: More caffeine | Dark Roast: Less caffeine

-Altitude and Shade apparently make the coffee better (but with more caffeine):



Marco Schille

I would be interested in the differences in brewing - too high temperatures bad / what effects does it have on the actual incredience of the final product? the best coffe I had in the south of europe and they apparently use high pressure low temperature for the espresso? Also there seems to be a common consenses that one cup per day is good - Is this the same like the wine "myth" - people who make the studies look for evidence that one glass is not bad / maybe even good?

Joe Rogan has a great podcast episode with coffee expert Peter Giuliano, he says that 195 to 205 degrees fahrenheit will give you the best tasting coffee. As far as what that does to the compounds in coffee, you might find something about that in the paper I referenced in response to the earlier question from Jorge Janke. As for what pressure / temperature for making the best espresso, I haven't come across something on that, but the owner

of Bear Pond coffee in Shimokitazawa Tokyo apparently is constantly changing variables like that to try and come up with the best espresso. He appeared on the documentary "A Film about Coffee," and the narrators were very positive about his coffee, but if you look at actual reviews for the place, it's pretty mediocre at 3.3 stars. It's pretty close to where I am so I guess I should check it out.

There's a lot of studies on coffee and health, and while most of them seem positive, there are some that say coffee is bad for cardiovascular health and studies like the "ATTICA" study have found that coffee provokes inflammation. But surely one of the reasons we see so much varying data on coffee is because people react differently to coffee. For example a 2008 study found that "a polymorphism in DRD2 (gene) (rs1110976) was associated with caffeine-induced anxiety in the Caucasian subjects"[Rb] Give me just a minute, I'll get more into this in depth in my answer to another question in a moment.

Hetynne

Differences between instant, pre-ground, and freshly ground brews on health. What happens when approaching overdose threshold? How long is the consensus cold turkey period before resetting your tolerance to caffeine?

-Since insoluble particles have to be removed before drying the coffee into a powder, you'd be missing out on certain flavor aspects and maybe beneficial compounds. The temperature reached during the drying process is actually higher than a typical roasting temperature, so you will get further degradation of for example trigonelline and chlorogenic acids.

The main health detriment I could find of instant coffee is that it decreases intestinal iron absorption more than drip coffee, but it's not that much worse than normal coffee. One study found that intestinal iron absorption went from 5.88% to 1.64% with drip coffee then .97% with instant coffee.

-As for pre-ground coffee, Pre-grinding <u>speeds up oxidization</u> of the compounds within the coffee - not a good thing. Apparently a lot of the aroma is lost as well.

-As for approaching the overdose threshold, I'm not quite sure what you mean, maybe you mean what happens as you approach the amount of caffeine that will kill you? According to this paper titled "The impact of coffee on health," [R*], 20 cups of coffee can "inhibit cyclic nucleotide breakdown via inhibition of phosphodiestarases," which may give a Viagra-like effect.[R,R] (Definitely not something I recommend... don't know if I could feel sexy in a dehydrated anxiety attack heart racing state). 40 cups of coffee are necessary to "block GABA receptors," and 100 cups of coffee can "mobilize intracellular calcium stores via activation of ryanodine receptors." 100 cups of coffee is around where you die. -According to thecut.com, a week: "Coffee researcher Joseph Rivera, the founder of Coffee Chemistry, suggests reducing your intake by half for a few days, then halving that for a few more days, and so on. "After about a week you should be pretty much back to how you were without drinking caffeine," he says." Personally, I've been just been reducing the amount of dry coffee beans I grind by 1g a day and have hit a kind of sweet spot at 15g (brewed with about 300g water) and haven't noticed any withdrawal effects by weaning off like this.

Coffee withdrawal headaches & Caffeine tolerance

"x" for a butthole

I always wondered why people who drink coffee regularly get headaches when they miss one morning's dose

People with a caffeine habit of as little as 100mg per day - about one cup of coffee, can start to get headaches and feel fatigued 12 to 24 hours after stopping. Why? "Chronic caffeine use results in an adaptation of the vascular adenosine receptor system presumably to compensate for the vasoconstrictive effects of caffeine." Basically, chronic caffeine consumers' bodies adapt to the fact that it can expect a dose of caffeine every day.

One of the effects of caffeine is vasoconstriction, so the adaptation that reverses that vasoconstriction still does it thing when the expected caffeine doesn't come in. Headaches are usually due to vasoconstriction or vasodilation. We can say that caffeine withdrawal results in a vasodilation headache as "withdrawal headaches among caffeine users correspond with increased CBF (cerebral blood flow) following 20-24 hours of abstention from caffeine."[R] <This study is very interesting if you're interested in how much we can tolerate.

What's interesting is my Mom sometimes gets headaches from too much caffeine, that may be a vasoconstriction headache as the body hasn't adapted to be ready for the level of vasoconstriction that amount of caffeine is triggering.

Scott Johnstone

What about caffeine tolerance?

Caffeine tolerance is very common and develops quickly, but it depends on the person/genes.

As per the paper titled <u>Genetics of caffeine consumption and responses to caffeine:</u>

"Tolerance to its acute effects develops rapidly, such that the effects of caffeine in habitual consumers are quite different from caffeine-naïve individuals. Physical dependence can develop, and withdrawal symptoms occur upon discontinuation of regular caffeine use. ...Likewise, certain individuals may be more vulnerable to the long-term negative health effects of caffeine. For example, while the pressor effects of caffeine attenuate rapidly in most consumers upon repeated intake, tolerance remains incomplete in certain subjects

...Animal studies show that chronic administration of caffeine produces multiple biochemical changes, including increased densities of A1 receptors, muscarinic and nicotinic receptors, and increased benzodiazepine receptors associated with GABAA in the brain. This

upregulation is thought to be responsible for the tolerance to the drug's effects."[\mathbb{R}^b]

Non-Caffeine effects from Coffee

Rolo

If there any effects not related to caffeine

Rafael Lourenco Cintra

Any benefits on drinking decaffeinated coffee instead of regular one?

Yes! The autophagic effect of coffee found in the study by Dr. Guido Kroemer & colleagues still occured with decaf too. There are several compounds in coffee like cafestol and kahweol which have beneficial effects for the liver. I talk more about this later in the question about coffee enemas.

Acrylamide

Matthias Forsberg

The fact that the beans are roasted, which creates Acrylamide - if the levels of this substance are high relative to other foods with acrylamide such as potato chips.

I wouldn't be too worried about Acrylamide.Looks like, depending on the (Swedish) person, coffee contributes about 20% of dietary Acrylamide whereas crisp bread contributes 28%.[R] My friend Misha wrote a interesting piece on <u>fact-checking/Acrylamide</u>.

Coffee Teeth Stains

Gary Silco

Discolor teeth or affect enamel?

Yes, coffee will stain your teeth.

This study from 1978 says that coffee *does* promote discoloration (only short abstract available, full text is behind a paywall.)[R]
This study found that, at least with tea, the casein in milk could prevent teeth discoloration, though they didn't look at coffee.[R]

According to Colgate...

"your tooth enamel contains microscopic pits and ridges that can hold particles of food and drink. Pigments from dark-colored drinks such as coffee, tea, and soda can become embedded in those cracks and ridges and, if the proper steps are not taken, can cause permanent, yellowing stains on your teeth."

It seems to be the tannins in coffee that cause the staining.[R] This study suggests the staining effect of coffee is *worse* than cola or tea.[R]

-If you're concerned about whether to drink coffee after tooth whitening... This study found that specifically after teeth bleaching at home, coffee didn't induce any statistically different staining compared to control. There was staining observed with red wine, tea and cola. "Following tooth whitening, patients should avoid drinks that cause tooth staining, particularly red wine, tea and cola." [R] This study found that coffee did cause some staining after bleaching, but red wine was worse. [R]

By the way, a girlfriend of mine said she didn't drink coffee to preserve her teeth, and she did have very nice looking teeth.

Coffee Enema

Dubh Glas

Maybe briefly look at coffee enemas too, if the science of benefits there is real or quackery!

Given there are some risks associated with coffee enemas, what I wonder is why people don't just drink their coffee and have a normal enema separately. It has been found that the cafestol and kahweol in coffee activate the detoxifying enzyme, glutathione S-transferase in laboratory animals.[R] However, what is the benefit or detriment of anal delivery of coffee rather than oral delivery? I haven't come across any benefits, but one detriment is that you may be absorbing less of whatever beneficial compounds are in there as this is the case with caffeine: "In summary, the relative bioavailability of caffeine obtained from the coffee enema was about 3.5 times significantly less than those of the coffee consumed orally." [Ra]

A quote from [R^a]:

"According to the Gerson regimen, caffeine from the coffee enema is believed to cause dialysis of toxic products from blood across the colonic walls or to cause dilation of the bile ducts, which in turn facilitates the process of elimination of toxic products from the liver. Nonetheless, none of these claims regarding the production of substantial health benefits by coffee enema and other colonic cleansing treatments has been supported by scientific research [7–9]"

The Gerson regimen, by the way, was developed in the 1930's as an alternative cancer treatment. "It involves consuming fresh, raw fruit and vegetable juices, eliminating salt from the diet, taking supplements such as potassium, vitamin B12, thyroid hormone, pancreatic enzymes, and detoxifying liver with coffee enemas to stimulate metabolism. ...Despite proponents' claims of recovery rates as high as 70% to 90%, case reviews

by the National Cancer Institute (NCI) and the New York County Medical Society found no evidence of usefulness for the Gerson diet."[R] Sodium restriction is already a bad idea, and since coffee will deplete it more, these patients were kind of lucky to get their coffee in enema form since they'd absorb less caffeine and perhaps have less sodium depletion.

Another quote from [R^a]:

"The documented potential risks of coffee enema include rectal burn induced by hot enema fluid, proctocolitis, polymicrobial enteric septicemia, electrolyte imbalance, or even death."

The rectal burn is obviously a result of insufficiently cooled fluid, but even correctly performed coffee enemas can induce complications like proctocolitis .[R]

■This study suggests there are no beneficial antioxidant effects from a coffee enema compared to drinking the coffee. Title: "Antioxidant effects after coffee enema or oral coffee consumption in healthy Thai male volunteers." [R]

There may be some truth to the idea that coffee enemas have some distinct "clearing out your system" properties. "Coffee enemas are believed to cause dilatation of bile ducts and excretion of bile through the colon wall. Proponents of coffee enemas claim that the cafestol palmitate in coffee enhances the activity of glutathione S-transferase, an enzyme that stimulates bile excretion." [R] This study was looking at coffee enemas as a candidate for clearing out dark bile from the small bowel for better visibility during a video endoscopy. They found that in distal segments of the small intestine, visibility was much better in the coffee enema group suggesting better clearance of bile fluid. However, this is for the specific purpose of improving visibility during an endoscopy. What would be interesting to see is what would happen if they had people simply drink coffee then give them a normal enema.

In any case, coffee enemas don't sound like a good idea. Just drink it, it tastes better that way .

Coffee & Longevity: Is it the Coffee or the Person? Christofer Lindgren

Thinking of studies linking coffe intake to longer life, decreased risk of cancer etc: Certain people (anecdotally) refrain from coffee consumption due to it causing or aggravating GI tract issues. May it be that coffee drinkers have more robust GI tracts and thus tolerate coffee better and also run a lower risk of disease and death, due to (I guess largely genetically) more robust internal organs?

This is a great question, and something I was wondering myself - is it that people who drink a lot of coffee become healthy thanks to the coffee consumption, or are they already healthier meaning they can withstand consuming massive amounts of coffee without bothering side effects. (This is in response to studies like this saying "In this large prospective study, coffee consumption was inversely associated with total and cause-specific mortality." [R]

It's most likely like the rich get richer, the healthier get healthier - because they're healthy enough to withstand the detrimental effects of coffee, they can get more of the beneficial compounds in it.

For example, I remember feeling pretty wretched- "wired and tired" when I was working as a consultant chugging coffee all the time so I ended up cutting back naturally at some point. Lately, I've gone from about 3 cups of really strong coffee to 2 cups of coffee half as strong as that and I feel much more calm, content and focused. Drinking too much coffee with cream/milk or drinking coffee too close to exercising gives me acid reflux-I'm not sure if I've ever gotten acid reflux outside of these situations. One night recently, I drank a lot of decaf coffee with cream and that really gave me acid reflux. (Hence, the dairy + coffee might be in cahoots to get me to the point of having acid reflux.) Black coffee makes me feel particularly

anxious and dehydrated, especially if it's cheap non-organic coffee. I feel best on butter coffee or coffee with a tiny bit of milk, and if I have coffee after 3PM or so it just makes me tired, and I'm pretty positive that a certain amount of coffee (usually the third cup of coffee brewed w/ 40g dry beans & ≈600g water) gives me inflammation, considering it gets difficult to breathe through my nose (nasal lining inflammation). There is evidence that coffee provokes inflammation (ATTICA study[R])

Anyways, the point is: I don't think a person like me is a good candidate for better longevity through slamming a bunch of coffee considering these effects. Will coffee *reduce* my lifespan/healthspan? Another hard thing to say, but as I do this coffee reduction experiment I'm feeling better the less coffee I have.

As per <u>Genetics of caffeine consumption and responses to caffeine</u>[\mathbb{R}^b]: "There are pronounced individual differences in response to caffeine. For example, some individuals are susceptible to its anxiogenic effects and others to caffeine-induced sleep disturbances and insomnia. Caffeine can aggravate anxiety and precipitate panic attacks in patients with anxiety and panic disorder, which often results in decreased consumption in these individuals. Individual differences in responses to caffeine may occur at the metabolic (pharmacokinetic) or at the drug-receptor level (pharmacodynamic), and they can contribute to the quality and magnitude of direct drug effects as well as to consumption of the drug. Likewise, certain individuals may be more vulnerable to the long-term negative health effects of caffeine. For example, while the pressor effects of caffeine attenuate rapidly in most consumers upon repeated intake, tolerance <u>remains incomplete in certain subjects</u>. Hypertensive subjects have been shown to be more likely to experience rise in blood pressure after caffeine consumption even with repeated administration. It is likely that several factors contribute to individual differences in responses to caffeine, including demographic and environmental factors such as age, other drug use, circadian factors, and sleep hygiene. One important source of

variability that has received some attention in recent years is genetic predisposition."

So, to answer your question, I think it's a little bit of both: The people drinking more coffee and living longer are healthy enough in the first place to withstand more coffee, so they can get more benefit from more coffee.

I need to figure out a way to get a 23andme done from here in Japan: "Childs et al. (2008) found that a polymorphism in DRD2 (rs1110976) was associated with caffeine-induced anxiety in the Caucasian subjects. An interaction was reported between ADORA2A rs5751876 and DRD2 rs1079597 that was associated with higher anxiety than either polymorphism alone."[Rb] I don't get intensely anxious from coffee so maybe I don't have any of that.