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On January 14th, I received an email from a concerned parent. We'll call her "Debbie". Debbie was her real name, but for litigious purposes, we'll pretend it wasn't.

Her teenage son had begun taking a supplement called "Pump Fuel". In her email, she asked me all the usual questions (e.g., "is it safe?").

My response was a little bit abusive. I told her she was right to be skeptical, gave her some reasons to validate her skepticism, and then followed up with this:

i don't understand why everyone feels so compelled to find chemicals to do what the barbells were designed for. tell your son to just work out harder. seriously. that might sound mean, but it would be far meaner of me not to say it. if i said "oh, the supplement probably won't hurt him" (or some such dismissal of the real point), he'd go out and buy it, waste his money, waste his time, gain nothing, possibly damage a few mitochondria, and more importantly, no lesson would be learned.

so just tell him to work out harder. and if he needs something to energize him into that level of intensity, tell him to drink a cup of coffee. if he needs more than that, tell him to drink two cups of coffee.

if he's not working out hard enough (and i doubt he is), there's no supplement that will do anything for him.

"Debbie" never wrote me back.

The advice I was vicariously issuing her son (*why do you need a supplement to do what barbells were designed for?*) should be central to the critique of any supplement.

Here, however, we have a supplement that doesn't work in the first place.

This should surprise no one.

Anyone who has read the label of "Pump Fuel" and then went on to buy it should be ashamed. And that shame should have no end.

Where the label isn't just a bunch of totally meaningless sentences (e.g., "premium pre-workout solution formulated with the highest quality ingredients for maximum product efficacy"), it's explaining to me exactly how worthless the supplement is (the ingredients list).

It's a little bit of caffeine and then a bunch of stuff that does nothing helpful whatsoever. It does have creatine in it, which would be helpful, but it's a negligible amount of a shitty version they're pretending is biologically superior by giving it a fancy name.

All in all, it's just one more carton of worthless powder marketed with the strategy: *take advantage of peoples' misunderstanding of what nitric oxide is and does.*

Nitric oxide is complicated. You're not expected to know what it is and does. Most physiologists don't. That's why there's a whole journal called *Nitric Oxide*.

Feel free to take a look: <http://www.journals.elsevier.com/nitric-oxide-biology-and-chemistry/>

It's been in circulation since 1997 and new articles continue to appear in every single issue.

There's a lot to know about it.

Have I read all of the articles? No. Of course not. Not even the editor of the journal has. I've hardly read any of them. But I've read enough to know that the purchasing of any nitric oxide supplement should induce incredible buyer's remorse.

The rest of this article is my attempt to explain "enough" so that no nitric oxide marketing campaign will ever tempt you.

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Usually NO-anything (Explode, XNO, NO-XS, Nitrox, MegaNO₂, Nox, Nitric Boost, etc.) in supplement form is just a bunch of arginine. And arginine is just an amino acid. Like all amino acids, it does a lot. It's involved in a lot of bodily functions. One of those functions is the production of nitric oxide.

My compliment to nitric oxide is this: it has a cool name.

It sounds very serious.

But unless your problem is erectile dysfunction (which might be a serious problem), supplementing nitric oxide isn't going to do much for you. Certainly nothing helpful. Nothing in the way of muscle development. It may do some harm though, if that's what you're after¹.

I guess it could be harmless enough if you were taking heaps of antioxidants at the same time.

“Okay, Courtney. I think I see where you're going with this. Alongside every scoop of nitric oxide, I should be taking a heap-matched handful of antioxidants. And then I'll be set. Yes?”

No, reader. No.

A) I just told you nitric oxide doesn't do anything helpful (turgidity aside). And B) even if it did, the answer is still no.

If you take your NO around your workouts (this is a bad idea; it actually wouldn't be such a bad thing to ingest if you didn't work out until all of it cleared your system), that would mean the simultaneous antioxidants were being ingested around your workouts. And if you take a bunch of antioxidants around your workouts, you're blocking the pathways for the breakdown products that provide signaling to create an anabolic response (inhibition of myostatin, etc.).

I realize that was a big sentence. Basically, if you take a bunch of antioxidants, you block a signaling cascade which, if blocked, stops you from making gains.

(Take-home message: you shouldn't be taking antioxidants around workouts.)

But this article isn't about antioxidants. It's about NO. Which means I seem to be steering down a giant tangent. I'm not. Later in this article, you'll understand why the antioxidant stuff is relevant to NO.

But we're not there yet.

¹ There's more than one mechanism for harm. The remainder of the non-foot-noted portion of this article discusses metabolic harm, but an abundance of NO in the cartilage is a problem too. A problem considerable enough to merit a footnote. This footnote: if a bunch of NO finds its way into your cartilage, you're looking at degraded fibronectin, which is what the integrin holds onto. And integrins are what run your mechanical feedback loops, which allow your soft tissues to be kept “in the loop” on your activities. Interrupt these loops and you'll find yourself in a remarkably catabolic environment.

Having said that, no NO supplement is regulated by the FDA, so you have no real assurance that what you're scooping into your pre-workout shake is going to affect your NO levels at all. What you *can* be sure of is that no non-regulated supplement is going to put NO binding protein into their product. It'd just be a waste of money when they could charge the same price without it and nobody would know the difference (especially since the people buying it don't even know *that* the binding protein would be useful). Without it, I don't know how long the supplement would be able to last in your body (or whatever tissue it might actually manage to penetrate).

But the point still stands: years of exposure might degrade cartilage. If there wasn't so much redundancy in the receptors, you'd probably see NO blockers in the health food stores, marketed as anti-arthritis supplements. The problem is that there's just so much overlap in mechanobiology and all the healing physiology. If you block NO for the sake of cartilage health, you might be inhibiting a helpful cell signaling cascade somewhere else.

So it's probably not worth blocking nitric oxide either. The best thing you can do is just leave it alone.

We've barely even talked about you. So let's start there.

You, reader, are an exerciser. And your workouts aren't free (in terms of metabolism).

The price tag attached to each workout is paid for by every one of your metabolic pathways. You can never completely isolate one pathway, shutting off the others. As long as you're alive, every pathway is continually running.

And the burliest of these pathways is your oxidative metabolism. Oxidative metabolism is why you breathe. Without it, you wouldn't need lungs.

This giant, extremely important pathway ends with what's called the electron transport chain. Here (in the electron transport chain), pairs of hydrogen (i.e., electrons) bind and unbind to a series of molecules in the mitochondria with a progressively increasing affinity in order to create energy.

Because the hydrogens are toppling down the affinity gantlet in pairs, and the terminal bond is with oxygen, the ultimate result is H₂O. Water. Water and a bunch of energy.

Peter Mitchell (a British biochemist) won a Nobel Prize for figuring this out.

Does all of this make sense so far?

"No."

Okay, sorry. Let me start over.

A mitochondrion is where all of your energy is made. Think of a mitochondrion like a tiny dance floor.

The electrons are the bachelors. It's a little bit gay that the bachelors are all showing up in pairs, but there's nothing wrong with that. Plus, the analogy will get a little bit weirder when you realize that the goal of every pair of bachelors is to have a threesome with the prom queen (oxygen).

So we have pairs of bachelors (hydrogen) showing up to the dance floor (mitochondrion), trying to tag-team the prom queen (oxygen).

But these bachelors can't just race to the PQ. The chaperons would report it as sexual deviance... and even if it doesn't result in criminal charges, there's going to be problems on some level. So for the most part, the bachelors all follow the rules. They work their way across the dance floor, mingling with some of the more common ladyfolk en route to the PQ.

They dance with the first girl for a moment, see another that looks sexier (more electronegative), break stride with the first, hook up with the second, see an even sexier girl, trade up again, and so on.

If you count NADH (the girl that drove you to the dance... you definitely owe her a couple steps), there are four total dance partners pre-PQ.

The fourth (cytochrome oxidase, which we'll call the maid of honor) is the girl that passes you (you and your buddy) to oxygen (the PQ). PQ is the last bond.

The three of you join in plural matrimony and live happily ever after.

The problem is that the electron transport chain isn't flawless. Those chaperons aren't going to stop *all* of the deviants. Once in a while, a pair of bachelors will start mingling with the bridesmaids and break some of the rules. The mess this makes is called superoxide (a free radical).

It's not the *only* free radical. Nor is it the most potent. There are worse crimes and criminals than sexual deviance and its deviants. But... can we go back to science now?

Do you get the whole "electrons working their way toward oxygen" thing?

Basically every time a pair of bachelors breaks stride with a bridesmaid, energy is released. They do it several times until they bind with oxygen. The ultimate result of a successful electron transport chain is water and energy. And when it gets messed up, you wind up with free radicals.

"Okay, yeah. That makes sense."

Okay. Well when you get a bunch of free radicals in your system, they're going to bounce around, crashing into stuff, modifying gene expression, causing cell damage, and ultimately putting you at a higher risk for cancer and a bunch of degenerative diseases (or at least it appears as though they have this effect) while ramping up your rate of biological aging.

Luckily, your body is pretty competent when it comes to superoxide cleanup. If released in reasonable quantities (like a standard high school dance), your body can generally turn it into hydrogen peroxide, then turn that hydrogen peroxide, then use an enzyme called catalase to turn that into water. Not quite water-to-wine stuff, but this has the perk of being true. And the result is your chemotherapy and geriatric care facility are kept at bay.

With me so far?

"Yes, Courtney, I'm with you."

Good. Moving on.

Not moving on as far as nitric oxide yet though. We'll get there. We're moving onto exercise first... because the only reason people take NO-based sports supplements is for exercise (or "sport").

So you, reader, are in the weight room. You haven't taken any nitric oxide (i.e., heap of arginine) yet, but you're getting in a pretty good workout anyway.

Remember that high price tag I said was associated with these workouts?

This is paid for by a drastic increase in the rate at which hydrogens are flailing down the electron transport chain (bachelors are shooting across the dance floor). And, predictably, this drastically increases the rate of superoxide production (sexual deviance).

A few of those superoxides escape your body's attempt to convert them into water, but still not the end of the world. Your body is durable. It can tolerate this.

Now, take that same workout, but introduce supplemental nitric oxide.

NO on its own is a weak free radical. By itself, it won't give you cancer. This is why I said taking it while you're not working out is probably okay.

But when you *are* working out, that NO is going to squeeze itself into the final pre-oxygen binding site (cytochrome oxidase, i.e., the maid of honor). While here, it will compete with oxygen for those hydrogens. And the harder you work out, the better odds it has at winning.

As NO starts binding to the hydrogens, something funny happens: the electron transport chain gets totally fucked up (enters into an extremely electron rich state).

When this happens, superoxide begins to be churned out in greater quantities. Much greater than would be happening with exercise alone. And, depending on exercise intensity and NO dose (etc.), that quantity is probably too much for the body to convert back to water.

So they start bouncing around your system.

And guess what else you have in your system?

Nitric oxide. Probably a lot of it because the *MuscleTech* scoop isn't small.

And guess what happens when nitric oxide meets superoxide?

Guess.

Right! It forms peroxynitrite!

And do you know what this is?

Right! It's the mother of all free radicals. It deforms practically everything it comes into contact with.

Enjoy the premature hospice. Or at least the metabolic dysfunction, as the peroxynitrite is formed in the citric acid cycle, which is where you actually burn your fat. That's where it's bouncing around destroying stuff.

Take-home message: don't ingest nitric anything (Boost, XS, Explode, etc) unless you're using it to overcome a bout with erectile dysfunction².

² Or if you're sneaking it into your workout partner's drink like some sort of lifting ruffie. But if that's the goal, don't stop with the altering of benzodiazepine (ruffies, not NO). You might as well hit all the transmitters. Or, opposite that, if you want a supplement that actually does something useful for you, find one that blocks gamma aminobutyric acid (i.e. GABA) rather than enhances it. We'll call this supplement "anti-ruffies". You'd find some serious results there. You might (temporarily) go insane from all the uninhibited cognitive stimulus (constantly noticing everything, like that you're wearing socks, and unable to stop noticing), but you'd be ferocious in the gym.

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Reader question (March, 2013): *I have my best workouts when I use nitric oxide and I always get a huge pump. I've read that muscle growth is limited by the sheaths around the muscle and they need to be stretched out for the muscle to grow and that's what the pump is doing and nitric oxide helps do that.*

While there was no question mark anywhere in the “question”, those were sentences to which I owe a response. Mostly because I’m curious what the literary material is that precipitates the “question.”

“I’ve read that...” doesn’t tell me what the sources are that are being consulted. And I suspect they’re just advertisements. A bunch of product claims that have never been evaluated by the FDA (or otherwise tested in any way). And of course these ads will tell you all the ways in which their supplement will make you huge. That’s how they take your money.

Open up a decade-old magazine though and you’ll see NO claims like this: hemodilation.

The ads claim that nitric oxide does that. It does hemodilation for you.

Outstanding. If this actually did happen, nitric oxide would probably be lethal. Hemodilation means expanding the volume of your blood cells. If you swallowed some solution that systemically dilated your blood cells, and those cells managed to not burst, the metabolic effect would probably be comparable to sickle cell anemia. I’m no expert here, but that would probably be bad. Luckily, claims like this are total nonsense.

In the last decade, the armory of “claims we hope you don’t understand” has become a bit more sophisticated (i.e., harder to understand), but no more accurate.

What nitric oxide does do is *vasodilate*. It dilates your blood vessels. So yes, if the supplement manages to work, it should open up your vessels a bit and that may lead to a bigger pump. But why is that something you’d want? When you’re doing a supplement-free workout, the diameter of your blood vessels already increases to a level beyond what is helpful. Why would you want to compound that? Your muscle won’t thank you. Circulation gets messed up, contractility is interrupted, etc. What you think of as perks aren’t perks.

Reader question (March, 2013): *Have you ever taken it?*

Interesting question.

People send me free supplements all the time because they want me to write about them. I can’t tell you how many nitric oxide supplements have been given to me. But I can tell you how many scoops of those supplements have entered my mouth. I’ll give you a hint: there’s no Roman numeral for this number.

-Courtney Jensen