THE TOX LAB

Podcast Transcript

Episode 9: New Year, New Risks: The deadly side of fitness fixes

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TRANSCRIPT

Hi everyone, welcome back to The Tox Lab. I'm Rebecca.

I'm Rob. This week we're going to be looking at a couple of cases where New Year fitness fixes went badly wrong: a caffeine overdose and a fatal case involving 2,4-dinitrophenol.

Before we jump into that, how was your Christmas?

It was good, thanks. How was yours?

Not too bad. Did you eat lots of sugar?

Of course.

And have you made any New Year's resolutions?

I don't tend to make them, because I usually break them within the first week, so I mostly avoid the whole thing. What about you?

Why don't toxicologists make New Year's resolutions?

I don't know.

Because they already know how dangerous too much of a good thing can be.

That is a poor joke.

The theme this week is very much "new year, new me." It's the time of year when people set fitness goals, promise themselves they'll be healthier, and often start looking at supplements to help get them there.

So this week we're going to look at two cases involving products linked to weight loss or gym performance.

The first involves a compound most of us know very well: caffeine. It is found in tea, coffee, cola, energy drinks, all sorts of things. It is probably the most widely used psychoactive compound in the world.

I would agree with that. I think most people need it just to function.

I certainly do. But another setting where caffeine comes up is in the gym, particularly in pre-workout products. People take it because they want an extra boost to sustain a workout.

So Rebecca, why don't you tell us a bit about caffeine and how it works, and why people use it for exercise?

Caffeine, also known as 1,3,7-trimethylxanthine, is a central nervous system stimulant. It mainly works by blocking adenosine receptors. Adenosine is one of the things that makes you feel sleepy or slowed down, so if you block it, you feel more awake and alert.

Caffeine can also increase alertness, improve perceived energy, and enhance some aspects of physical performance.

It has been shown to improve athletic performance in both aerobic and anaerobic activities. Doses around 3 to 6 milligrams per kilogram can improve sprint performance, cycling and running time trials, endurance, and even measures of muscular power. It can also reduce perceived exertion, meaning a workout feels easier than it otherwise would.

So on paper that sounds ideal. More energy, better performance, maybe one or two extra reps, slightly more endurance, exactly what somebody chasing fitness goals might want.

Exactly. But caffeine also has a darker side when the dose gets too high.

So let's look at the first case.

The paper is titled Dangerous mistake: accidental caffeine overdose and was published in 2018.

In this case, a 32-year-old woman presented to the emergency department complaining of malaise, anxiety, dizziness, and nausea. At first, her examination was not especially dramatic. Her blood pressure was normal, her heart rate was initially acceptable, and the only clear abnormality was a mildly raised glucose.

But then she developed a near-fainting episode, became very agitated, started vomiting, became pale and sweaty, and was found to have a tachycardia of about 160 beats per minute.

Her arterial blood gas showed metabolic acidosis and severe hypokalaemia, meaning a dangerously low potassium. She was treated with intravenous propranolol, which resolved the dysrhythmia and helped correct the metabolic abnormalities.

It turned out that she had made a mistake when preparing her pre-workout supplement. She had used the same scoop she used for protein powder, so instead of taking around 300 milligrams of caffeine, she had taken approximately 5,000 milligrams, or 5 grams.

To put that into context, a normal cup of coffee might contain something like 75 to 150 milligrams of caffeine. So 5 grams is an enormous dose.

And doses in that sort of range, 5 grams or more, have been fatal in other cases.

So what sorts of toxic effects do you get from caffeine?

At the milder end, people will be familiar with jitteriness, palpitations, anxiety, tremor, nausea, maybe not being able to sleep.

At the more severe end, you can see marked tachycardia, dangerous arrhythmias, seizures, rhabdomyolysis, and electrolyte disturbances such as hypokalaemia. That low potassium can itself contribute to the risk of serious cardiac dysrhythmias.

And what happened to this woman?

She was actually quite lucky. She remained on an intermediate care unit for about two days, had some persistent tachycardia, and needed a bit more oral propranolol, but ultimately she recovered fully.

So this is really an unfortunate dosing error. Protein powder is something you measure in large scoops, whereas pure or concentrated caffeine supplements are taken in much smaller amounts.

Exactly. And the paper apparently included photos of the scoops, and she really had got it very, very wrong.

I think scientists sometimes forget that we are quite used to thinking in dose and mass intuitively, whereas most people aren't constantly visualising what 300 milligrams looks like.

I have actually had a mild caffeine toxicity experience myself, nothing like this, but years ago I drank far too much caffeinated alcohol over the course of an evening and ended up with the most bizarre sense of impending doom. It was genuinely awful. Not fatal, obviously, but deeply unpleasant.

So yes: go easy on the caffeine.

The second case involves a much less familiar compound: 2,4-dinitrophenol, often abbreviated to DNP.

This is not approved for human consumption. It has a grim history, including use in industry and explosives-related manufacture, and it occasionally appears in weight-loss products.

So Rebecca, take us into the case first, then we can talk about what it actually does.

This case involved a 21-year-old bodybuilder. He first presented to his GP in early 2019 with painful gynaecomastia. A few months later he presented with sweating, tachycardia, fast breathing, gastrointestinal symptoms, and irritability.

Later that same year he presented again to hospital with dry mouth, vomiting, a heart rate of about 145 beats per minute, hypertension, hyperthermia, acute kidney injury, rhabdomyolysis, and a respiratory alkalosis.

About 15 hours after admission he admitted to using 2,4-dinitrophenol.

So what is DNP?

2,4-Dinitrophenol was recognised in the 1930s as an extremely effective weight-loss agent. People were losing large amounts of weight on it, but by 1938 it had already become clear that it caused severe toxicity.

The way it works is by uncoupling oxidative phosphorylation. Normally, your body breaks down fats and carbohydrates and uses the energy to generate ATP, the energy currency of the cell, through mitochondrial oxidative phosphorylation.

DNP disrupts that process. The body keeps burning fuel, but instead of efficiently capturing the energy in ATP, much of that energy is lost as heat.

So in simple terms, DNP turns your metabolism into a furnace. You burn calories very quickly, but you also generate huge amounts of heat and become dangerously hyperthermic.

Exactly. That is why it causes weight loss, but also why it is so dangerous.

After that first admission, he was discharged, but he continued to have symptoms like profuse sweating, tachycardia, and irritability. He denied chronic use and only admitted to a single episode of DNP ingestion.

Then, in 2020, he presented again after admitting to taking 2 grams of DNP around six hours earlier. He had fast breathing and respiratory alkalosis initially.

About nine hours into the admission, he started to deteriorate. He became confused and agitated, remained tachycardic and hypertensive, and his temperature rose from 37 degrees to 38 degrees and then continued

to climb to 41 degrees despite active cooling efforts.

His respiratory rate then dropped, he developed multi-organ failure, and unfortunately he died.

And that is really the terrifying thing about DNP. Once toxicity develops, there is no antidote. Treatment is essentially supportive and focused on aggressive cooling and organ support, but you can't easily switch the effect off.

At post-mortem, DNP was detected in blood at 88 milligrams per litre and in urine at 83 milligrams per litre. It was also detected in hair, suggesting repeated exposure rather than a truly isolated one-off use.

Interestingly, the hair analysis also detected a range of anabolic-androgenic steroids, which is not especially surprising in the context of bodybuilding and appearance-enhancing drug use.

One other interesting post-mortem finding was yellow discoloration of the feet. DNP is a bright yellow compound, and yellow staining of tissues has been reported in chronic DNP users because the compound can accumulate in fat-containing tissues.

So these two cases really show both ends of the spectrum. At one end you have caffeine, which is legal, familiar, and often relatively safe when used properly. At the other end you have DNP, which is profoundly dangerous and absolutely not something anybody should be using.

Exactly. Caffeine, used properly, is probably a relatively low-risk supplement for most adults. DNP is in a completely different category.

If you are thinking of using pre-workout products, read the label and be very careful about dosing. And if someone offers you weight-loss pills that sound too good to be true, especially if you have any suspicion they might contain DNP, avoid them.

So I think we're going to wrap this episode up there. I hope you've enjoyed listening.

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We hope you've all had a lovely start to 2025, and we'll see you next time. Bye.