

Episode 23: Death Coffee and Penconazole Toxicity

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TRANSCRIPT

Welcome back to the Tox Lab. I'm Rebecca. I'm Rob. This week, we're looking at a couple of case studies that caught our attention. The first case we're going to look at is a case of death coffee in Iran.

It had quite an attention grabbing headline. Do you like coffee, Rebecca? I do, I never used to, but now I'm slightly addicted. How do you like your coffee?

I'm just outing you as liking really sweet lattes. I'm partial to a latte, for sure. Bit of caramel syrup, you can't go wrong. But not death coffee.

Definitely not death coffee. So this was a case that came out of Iran, published very recently, wasn't it? It was a case series of individuals presenting to emergency departments, following consumption of what was known as or what was locally sold as death coffee. So Rebecca, why don't you introduce us to this case series?

This paper covers five cases from February 2024 to 14 April 2024. These included males ranging from 25 to 55 years old. Four out of five of them had no known pre-existing conditions, caffeine use disorder or substance misuse disorder. One did have a five-year history of psychiatric disorder and was on a variety of prescribed medications for this, including sodium valproate, quetiapine, perphenazine, and biperiden.

And all of these individuals presented to their local A&E departments between 30 minutes and three hours after consuming as little as half a cup of death coffee. So whatever this death coffee is, it sounds like incredibly potent stuff. It does, and they all experienced a variety of symptoms ranging from palpitations, dizziness, shortness of breath, blurred vision, restlessness and agitation. One individual experienced visual hallucinations, and one interestingly presented with sleepiness and decreased level of consciousness, which I thought was a bit unusual for what's supposed to be a stimulant overdose.

Yeah, so we covered caffeine overdose a few episodes back, didn't we? Yes, we covered this back at the start of the new year in episode nine, New Year, New Risks. So yeah, go and check out that episode if you want a bit more of a deep dive in how caffeine toxicity works, but essentially it's a stimulant. We're probably all quite familiar with caffeine.

It's everywhere. It's in tea and coffee. It's in Coca-Cola. It's in Red Bull.

You drink too much. The symptoms you experience tend to be stimulant related. They tend to cause palpitations, increased blood pressure, things like that. And all of these individuals were treated with some form of benzodiazepine.

So either diazepam or midazolam to alleviate their symptoms and help prevent potential seizures that clinicians were expecting might occur. But they all made full recoveries and they were all discharged, I don't think after a particularly extensive hospital stay. And it seems that all of these cases were put down to

caffeine intoxication.

So what is death coffee? Well, this paper doesn't really explain it, does it? No, it's quite frustrating actually. I really wanna know what they think death coffee is or what sort of caffeine content we're looking at.

Are we looking at something like three times the regular caffeine content or are we looking at something even more dangerous? So there is a brand of coffee called Death Wish Coffee and that claims to have the strongest caffeine content, although there might be contenders in that market now. And that, I believe, claims to be about three times the caffeine of a regular coffee. I'm pretty caffeine tolerant.

So my yardstick might not be the best to go by, but even if you're completely caffeine naive, three cups of coffee might make you feel a bit rough, probably won't put you in A&E needing benzos. So I'm not quite sure what's going on with these cases. It's really interesting that there seems to be some common link for them all. So I did have a chat to a friend of mine who's from Iran and she got in touch with a friend of hers who works as a GP and it does seem to be that this is a bit of a thing.

I'm not sure anybody really knows quite what is in death coffee. One rumor that had been flying around according to this contact is that people were fortifying coffee with other things and kind of marketing it as such. So it might well be there's other stuff in there. Yeah, the frustrating thing about this case series and all five of these cases is there's no results from any sort of toxicology screens.

So we are assuming that it's all down to like acute caffeine intoxication, but there could be something else there that we're just completely missing that explains how they've ended up in A&E. Four out of five of these cases had symptoms consistent with caffeine toxicity, including one who had only had half a cup of this strong coffee. So it does suggest that there really is quite a lot of caffeine in this. If caffeine is the sole culprit, it would have been really nice to have had a nice full toxicology screen just to confirm we weren't missing some amphetamines or something else.

I did want to drill into that one case that presented with very atypical symptoms, didn't they? So this case was a 55-year-old male who presented about half an hour after consuming a cup of death coffee with symptoms of restlessness, sleepiness and decreased level of consciousness. He was taking low-dose aspirin, though they don't specify what reason that was for. It was his first time consuming death coffee and he was a daily smoker.

His ECG on arrival showed premature ventricular contractions. All of his labs seem to be within normal limits. They don't define what those normal limits are. He had a heart rate of 101 beats per minute, respiration rate of 18 breaths per minute and a normal body temperature and was admitted to the ICU.

So he must have been really suffering and really quite unwell for it to be escalated to that. It's weird, isn't it? Something was clearly going on, but reduced levels of consciousness and sleepiness don't typically fit with what we see in caffeine toxicity. So as I say, I find it really hard to believe that half a cup of even very strong coffee, even if that coffee is three times as potent as normal coffee is likely to land you in the ICU.

So I do wonder if there is more to this case series. How do these cases compare to the case we discussed in episode nine in terms of the caffeine content? That was sort of grams, wasn't it? Really, really quite high dose.

Yeah, that was a pre-workout measuring mistake gone wrong. So it was significantly more caffeine, I believe, than what they're implying people were being exposed to in these cases. So interestingly, in the UK, there doesn't seem to be a legal limit for how caffeinated your coffee is allowed to be. Although if you're selling anything with a caffeine content more than 150 milligrams per litre, it is supposed to have a warning label saying "high caffeine content".

So it's interesting that some of this high caffeine coffee can just be sold freely, but I don't think this is what we're looking at here, as I said. Okay, so let's move into our second case report. So this is a case report out of Italy, I believe, and it's very, very different from the death coffee case. This is a post-mortem case report that had some very, very unusual findings.

Rebecca, why don't you introduce us to this case? So I do have to give a little warning before I start talking about this one. We are diving into the topic of suicide a little bit, so if that's something that you don't want to be listening to right now, please click off the rest of this episode. So this case involves a 73-year-old male who was found near death on the floor within a farmhouse.

He had an extensive sharp wound to the neck and a bottle of fungicide was also found near him. He was transported to hospital where his wound was sutured. He presented hypothermic with pinpoint pupils that were not reactive to light. He was also hypoglycaemic and had a metabolic acidosis with a raised lactate, and his blood pressure was only 65 over 60.

He had quite an extensive medical history, so he was suffering with AF, which is atrial fibrillation, cardiac stenosis, dyslipidaemia. He also had ischaemic heart disease, and he died shortly after admission to hospital. There seemed to be no history of psychiatric disorders, no substance abuse, and no previous attempts to end his life. This was all a bit out of the blue.

So an extensive medical history, although not an uncommon medical history, right? We see a lot of people who've got that sort of illness in the background. Yeah, nothing seems strange, especially for someone of that age. So this individual underwent a post-mortem and was found to have a wound on his neck that was eight centimetres by three.

They also undertook some toxicology testing and found penconazole, which is a systemic triazole fungicide. And this was found in both blood and urine at a concentration of 6.35 milligrams per litre in peripheral blood and 4.68 milligrams per litre in his urine. And they attributed the death to both the cut-throat sharp injury and penconazole poisoning. Triazole fungicides are a group of fungicides that act as demethylation inhibitors.

These act by inhibiting the enzyme CYP51, which blocks C14 demethylation during the biosynthesis of ergosterol, which is an important component of fungal cell membranes, and therefore the fungi can't grow and they can't develop and then they die. And that's how it acts as a fungicide. Interestingly, CYP51 is also found in humans and plays a role in cholesterol biosynthesis. I therefore can imagine that being exposed to this type of fungicide will affect steroid hormone synthesis pathways and things like that.

In terms of its toxic effects, there's not a lot of data out there that I could find anyway, researching this episode, on humans, but it's known to cause hepatotoxicity, including hypertrophy and steatosis. It can also cause cardiac toxicity and neurotoxicity. When this individual presented to A&E, he did have metabolic acidosis and what they think is an acute tubular injury was also seen at post-mortem. So that might indicate there's also a nephrotoxic effect in humans that hasn't been reported in animals at the moment.

It could be due to the production of reactive oxygen species and apoptosis that's going on in the kidneys. So this was really quite an interesting case, wasn't it? You've got two potential causes of death, a fatal neck wound and also a really unusual finding on toxicology. There isn't really much toxicology literature to compare that finding to.

As you say, there's a lot of theoretical toxicity. I was able to find some LD50 data. I can't believe we're on episode 20-something and we're only now just explaining what LD50 is. But an LD50 is an experimental way of expressing a compound's toxicity and it's the concentration of a substance that kills 50% of a given population.

So in this case, I was able to find an LD50 in rats for penconazole of about 2000 milligrams per kilogram. So really quite high grams of the substance per kilo of rat. On the other hand, it sounds like if there was a bottle found next to him, he possibly had consumed a very, very large dose. So what do we do as toxicologists when we're faced with this situation?

So often we're dealing with compounds where there's previous published case data, right? And we can simply refer to existing literature, and in this case we kind of haven't got that. So we're kind of forced a bit more to consider what we do know. Yeah, it is really hard when you quantitate a drug, when you've not got that much information on how toxic it is, to then look at that number and go: is this fatal?

Is this just a little bit toxic and kind of attribute some of the symptoms or things to that level? I think one thing that should be considered in this case and possibly it was, it simply wasn't addressed as far as I could see in the paper is that the Topaz brand of pesticide is actually about 40% penconazole. But the rest of the mix is actually kind of a carrier solution, it's mostly organic solvents. So things like naphthalene.

Naphthalene is actually incredibly toxic. Naphthalene, if you've not come across it, is what's in moth balls. And that can cause well-documented toxicity, including on the liver and the kidneys. So I do wonder, although clearly a very large dose of penconazole has been taken, whether actually some of the toxicity could have been attributed to other things in the mix itself.

So this case is really quite interesting, isn't it? It really is one of those cases where you've got two possible causes of death, and the toxicology is a good reminder of why it's important to still do toxicology in some cases even if you think you've got some obvious mechanical cause of death. But also, you know, how do you decide, or how does anyone decide, which is more likely? So it definitely speaks to the complexities of trying to determine a cause of death when you have multiple potential options, and it's impossible a lot of the time to know what kind of dealt that fatal blow.

It also shows how important it is to work with pathologists, isn't it, and work as a team. We all have individual pieces of the puzzle, right? We do need to collaborate to kind of get an idea of the cohesive overall picture. So I think both these cases kind of caught my eye with attention-grabbing headlines based on the title.

I do think possibly, particularly the first case, although perhaps a little bit in the second case as well, there may be a little bit more to these stories that isn't being explored. I do think it's important that, even though sometimes when we encounter cases or case series like this we don't know all the answers, they still get published, don't they? Because it does allow many more people to participate in the discussion as well as adding to the body of knowledge out there.

For example, if I ever see penconazole in the future, it'll be good to be able to refer to this case. I think one of the other things that this case made me think, actually, is that probably we don't publish enough case reports. I've been involved in a case of fatal pesticide poisoning, which is rather unusual. Probably we should try and write up more cases, as there really can be merit in some of these, right?

Yeah, I think it's important that if you are generating data that could be useful to others and meaningful in some way, that we contribute to that. Because you'll find a really interesting case report that helps you interpret something, and someone else could be looking for something that you have and if it's not out there, they can't use it. So I do think we should all be thinking about whether we've got interesting cases stuffed into a drawer somewhere that we've been putting off writing up that could actually be beneficial to the wider field. Yeah, I think that's completely fair.

With regard to the Iranian coffee case series, I do think that might be one to watch. Possibly there is something underlying here that could be the tip of an iceberg. And we might be looking at a bit of an outbreak, possibly. Yeah, it'd be interesting to see how that one develops.

Okay, cool. So I think we're going to wrap it up here. I hope you've all enjoyed listening this week. Do give us a like and a follow on social media.

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For those of you who don't use social media, we have an email. So you can email us at thetoxlab@gmail.com. You can find that in the description of this episode, as well as the links to the papers we've discussed today. Hope you all have an amazing week and we'll see you next time.

Bye.