Episode 53: From Cosmetics to Creatures - A Mix of Unusual Poisonings

Transcript

Hi everyone, welcome back to the Tox Lab. I'm Rebecca. I'm Rob. This week we're gonna be looking at five cases, all involving very different types of poison or toxin, looking at the breadth of toxicology. So Rebecca, a question that you should be able to answer.

You've been a toxicologist for a little while now. So you should know the answer to this and so I'm gonna put you on the spot. Oh no. How many toxic substances are there?

I don't think anyone can give you any except for that one. So people have tried to estimate it. There's the classic Paracelsus answer, isn't there? That everything's poisonous, it depends on the dose.

But in terms of estimates, people have tried to estimate it and we are looking at millions of known compounds and hundreds of millions, potentially infinite number of other chemical combinations that could be poisonous. So the number is absolutely huge. And this is relevant because I'm often asked, so Rob, how many episodes of the Tox Lab are you gonna do? Are you gonna run out of content soon?

Clearly, if there's millions of possible poisonous substances out there, we're not gonna run out of content. Before we jump into today's episode, if you wanna stay up to date with our content, you can find us on Instagram at @the_tox_lab. We also have a page on LinkedIn and we're fairly active on there. And for those of you who don't use social media but still wanna get in touch with episode suggestions or comments about our episodes, you can email us at thetoxlab@gmail.com.

So Rebecca, we've got five papers, haven't we? All five little cases, five completely different poisonous substances. Why don't we jump into the first one? So this first paper is a retrospective observational study of the medical tox service at Ceraski Medical Center in Tel Aviv on patients presenting with hair straightening treatment toxicity between the 1st of April, 2021 and the 1st of March, 2025.

Patients were included if they presented hospital with clinical manifestations of toxicity following exposure to a hair straightening product. And they also must have undergone a medical toxicology service consultation. In this time period, 13 female patients were admitted following exposure to a keratin based hair straightening product containing glyoxidic acid derivatives which have been marked as formaldehyde free. Patients age range from 15 to 53 years with a mean age of 22 and five patients were under the age of 18.

And these patients had visited a variety of different hair salons but did report undergoing either like Brazilian or an Indian hair straightening treatment. And these all use glyoxidic acid based hair smoothing procedures which then use heat to provide long lasting hair straightening. The average time from hospital admission to being reviewed by the medical tox service range from one hour to 36 hours with a median time of 24 hours. And the earliest diagnosis was established in a patient who presented soon after experiencing nausea and had also heard in the media about the potential toxicity of these products.

The time from hair straightening treatment to onset symptoms range from two to 72 hours. And the most common presenting symptom in these cases was vomiting which occurred in 12 patients. Other common symptoms included abdominal pain and scalp rash. Interestingly, 12 of these patients were

diagnosed with an acute kidney injury with the median current and concentration being 371 micromoles per liter while admission and this had decreased at discharge to 159 micromoles per liter.

They did take urine samples in three of these patients to look for calcium oxalate crystals which were positive. Eight of these patients did receive treatment with pyridoxine and thiamine and luckily in all of these cases hemodialysis was not required to treat. And this one really caught my eye actually as a headline. Yeah, it was really catchy, wasn't it?

The freely available hair straightening products actually leading to acute kidney injury. So traditional hair products contain formaldehyde which would denature proteins and allow them to reform in a new structure. Formaldehyde is now recognized as being quite carcinogenic and therefore there's a trend away from formaldehyde hair products to these newer glyoxalic acid products. These are marketed as formaldehyde free and you heat them up and they dehydrate and they sort of form ester linkages within the hair protein.

So reshape the hair without crucially using formaldehyde. But actually it looks like these replacement products might also have their own degree of toxicity. Now this is a small number of patients all presenting, isn't it? Relative to the number of people that are probably using these products but they're relatively serious symptoms, aren't they?

You know, the idea of acute kidney injury so a sudden drop in renal function as a result of a nephrotoxic insult. And interestingly, glyoxalic acid is also a metabolite of ethylene glycol, isn't it, antifreeze? And antifreeze, as we know, is quite poisonous and it's the glyoxalic acid that is the poisonous metabolite that is then converted to oxalate that leads to the toxicity of antifreeze. The idea that glyoxalic acid, therefore, is suddenly a safer alternative when we know it can be poisonous is quite interesting.

I think the logic probably is that if it's in your hair, it's not being systemically absorbed but actually, clearly these cases show that it possibly is to a degree. What's interesting as well actually with glyoxalic acid is in order to get it to work, you have to heat the hair up. And if you heat glyoxalic acid up hard enough, it decomposes to formaldehyde gas anyway. So these formaldehyde-free hair products are possibly not formaldehyde-free when used in the way that they're used.

They're really widely available though. You can buy these off the high street. They may not be the same products that these people have used here. There may be orders of magnitude concentration difference possibly or things like that.

I'm not saying that what you can buy in boots is unsafe but these are not under the counter, unregulated products. There are big brand name hair products containing glyoxalic acid. In terms of the study, it was only little wasn't it? There could be potential confounders and we haven't got a causal link but there is at least a plausible mechanistic link isn't there with glyoxalic acid to oxalate, oxalate being nephrotoxic and they were able to demonstrate oxalate crystals in the urine.

So surprising toxicity in a high street household products that many of us may use without even realizing. Okay, let's completely change gears and look at our next paper which is very different. So this next case involves a 21 year old shipyard worker with no significant medical history who was cleaning the hull of a vessel on the French Riviera returning from a Mediterranean circumnavigation. When he inserted his arm into a cavity on the ship he immediately experienced a burning pain radiating from the upper forearm to the elbow.

When he looked at his arm there were white filaments embedded in the skin and there was localized edema which developed within minutes. The cause of this appeared to be a worm known as the bearded fireworm and this was identified by a marine biology expert. The regional poison control

center was contacted promptly and recommended abundant rinsing and medical evaluation. The patient rinsed the area with sea water and then fresh water and self-treated with oral paracetamol.

He went on to experience burning pain for about 24 hours, edema for four days and itching for about three weeks without development of systemic symptoms. So he was cleaning a ship, put his arm in a hole and something stung him. I was surprised at how long the pain lasted. We're so used to, particularly in the UK.

In the UK, not a lot of stuff that stings you stings you that badly or that hard, does it? Yeah, we get a wasp sting, it hurts a bit. We don't have anything particularly venomous usually. So I was surprised at this one.

It's an interesting area, isn't it? Venom toxicology is such a niche area of study intersects with zoology and I'm gonna have to hold my hand up and say that venom toxicology is not a strong point of mine. It's not something we tend to get too involved in in the casework. Although maybe our colleagues in accident and emergency departments are dealing with this and not consulting the lab because let's be honest, I would be of no help.

I did get involved in a case some years ago which was a snake bite case and I was overwhelmed in that case by just how helpful toxicology colleagues in other areas were and it ended up me making friends with somebody from the Liverpool School of Tropical Medicine and it was a really humbling experience to know that there are just so many versions of toxicologists out there that have got specialist knowledge in all these areas. But in terms of this case then, what actually went on?

So bearded fireworms are thought to contain compounds such as carunculines which are butane-derived quaternary ammonium compounds and these seem to have been fairly recently identified in these sorts of worm species and that's what causes that like burning pain and the swelling and the itching. And this is a little bit worrying because the bearded fireworm is being spotted with an increased frequency in the Mediterranean. So there is the potential that it's gonna put more people at risk of being stung. Especially like swimmers and people hanging out on the beach in the Mediterranean which sounds lovely.

Until he gets stung by a bearded fireworm. Until he gets stung by a bearded fireworm. Yeah, so there seems to be this general migration up the East Coast of Africa, doesn't there, towards the Mediterranean, potentially expanding their habitat a bit. And these things have existed in tropical waters for a long time.

It's just part of life. It's just now that as they move into new areas, people that are not used to being aware of the dangers of fireworms or even healthcare workers that see a patient with a sting on their arm may not be aware that the fireworm could be a thing. So this was South of France, wasn't it? So a move from the West Coasts of Africa where they more traditionally were first identified.

But patient recovered okay, no long-term outcomes. And again, this is just a one-off case, isn't it? This is a single isolated case report. It's a nice little case report.

It isn't proof that suddenly there's fireworms everywhere in the Mediterranean. This isn't a case that says we need to panic. So this next paper is of a study that's looking at data from the National Poison Data System of American Poison Centers from 2000 to 2023 involving single substance exposures to Medadrine. So Medadrine is an oral alpha-1 adrenergic receptor agonist that's been approved by the FDA for treatment of orthostatic hypotension.

It acts as a prodrug and its metabolite desglymedadrine is selected for vascular post-junctional alpha-1 adrenoreceptors, which will increase peripheral vascular resistance by causing constriction of arteries

leading to an increase in blood pressure. In an overdose situation, this can lead to reflex, bradycardia, and hypertension. And while these effects may be rare, they're often really significant. So in this time period, 1,935 single substance exposures to Medadrine were reported, and these did increase over time from 21 exposures in 2000 to 171 in 2023.

They also looked at the number of people during this time period that were being prescribed Medadrine and even after adjusting for the increased number of people who had been prescribed it, there was still an increase in the exposures that were reported. 95% of course, the Poison Center had age information with 19% of exposures being from children under the age of five, 2.7% being from children between the ages of six and 12, 11 and a half percent involved 13 to 19 year olds, 29.2% involved 20 to 59 year olds, and 32.7% involved people 60 years or older.

Majority of exposures involved females, and 53% of the individuals were managed onsite with the remainder being referred to healthcare facilities for treatment. Common effects reported included hypertension in 14% and reflex bradycardia in 10%. Vomiting, headache, nausea, lethargy, dizziness, and chest pain were also reported fairly frequently. In some cases, more serious side effects were noted including central nervous system depression, seizures, slurred speech, confusion, and syncope, and one patient reported dysrhythmias.

In terms of therapy, IV fluids, activated charcoal, antihypertensives, and supplemental oxygen were given. In quite a few cases, 20 individuals received atropine and five ended up being endotracheally chipped. The side effects noted were reported with significantly greater frequency in those who had been exposed to Medadrine as a result of a suspected suicide compared to those that were exposed due to a dosing error. Unintentional exposures represented the largest reason for those under the age of six with therapeutic errors being the most common reason for those aged six to 12, 20 to 59, and those over 60.

And in the 13 to 19 year old age group suspected suicide was the most common reason for exposure. In terms of medical outcomes, these were known in 1,102 of the cases with 29% resulting in no effect, 10% minor effect, 18% moderate effect, and 0.6% were major effects with no deaths reported. In 45% of exposures, the level of healthcare received was documented with half being treated, evaluated, and released, 13.3% were admitted to critical care, 9.4% were admitted to a psychiatric facility, and 8.8% were transferred to a non-critical care unit.

And what was interesting is that the number of patients being dispensed Medadrine had increased by 700% over the time period between 2000 and 2023. So this is a drug that I must admit I hadn't heard of. I had to look it up, and yet it does seem to be increasingly prescribed. It's used to treat orthostatic hypotension, so when people have got low blood pressure when they stand up.

If you've got that as a condition, you can risk fainting and falling over and things like that. So it makes sense to try and treat it, and obviously Medadrine is one of those drugs that can do that. I was surprised, though, that the number of presentations they've had related to its toxicity, and it's probably a side effect, isn't it, of there being this increase in orthostatic hypotension, which is associated with autonomic dysregulation. So where parts of the nervous system don't work so much anymore.

And this can be associated with things like Parkinson's disease, but also quite a lot of drugs can lead to orthostatic hypotension. And so as we're seeing this older population and more polypharmacy, we're then possibly seeing this increase in the need to treat the side effects of that polypharmacy with drugs like Medadrine, and it's now seeing quite a spike actually in prescriptions. What period of time was that over? 23 years from 2000 to 2023.

Okay, so it's quite a long period of time to see a 700% increase, but nonetheless, it's quite significant, isn't it? I think it's probably one for us to keep an eye on actually, given the number of accidental exposures in children and the fact that it can be very significant. So this next article looked at a surveillance study of illicit substance toxicity using clinical data from all adult illicit drug-related attendances at the Queen Elizabeth University Hospital Emergency Department in Glasgow, and they also looked at surplus anonymized blood toxicology analysis from patients with moderate to severe toxicity at presentation.

Isocyanitazene, which is the 5-cyano analogue of isotonitazene, and its N-desethyl metabolite were detected using LC high-res mass spec in a sample from the same patient who attended the emergency department twice in the same week in early 2025. Both these samples did show evidence of multi-drug co-ingestion. On admission, the individual had a reduced level of consciousness and bilateral pupillary constriction, which is consistent with opioid ingestion and what we would expect from the N-desethyl metabolite. So we've moved back into my area, which is novel synthetic opioids.

And we've talked a lot about N-desethyl isotonitazene, haven't we? These are very potent opioid compounds. They act on the mu opioid receptor. They cause symptoms consistent with opioid toxicity in the same way that morphine or fentanyl does.

What's interesting about this one is we're calling it a nitazene. It's not really a nitazene anymore at this point, is it? We called them nitazenes because they had that nitro group. And really this one sits a little outside that original naming logic.

This doesn't have the nitro group and it's been replaced by a cyano group. So structurally, it's different enough to avoid detection by a lot of traditional detection systems. And probably some of the immunoassay-based techniques that are now available for testing for nitazenes, often in powders, may not pick this up. But functionally, it appears to behave like an opioid, as other nitazene analogues do.

This was a nice little single case presentation, wasn't it? Just showing that this compound is out there. It's actually collected as part of a wider study. The wider study that it was part of is this broad monitoring study where they take excess blood and see what people have been exposed to.

The fact that they were able to pick up this novel analog as part of that really does prove its value, doesn't it? That actually people could present to hospital with all sorts of intoxications. And unless you're actually looking, using a technique that can look for thousands of compounds, you might miss something new. There was no structured data or anything presented, was there?

Little bit disappointed that there wasn't some fragments and some structures that we can dive into. But it was a nice little single case presentation and crucially, again, shows us that this new opioid is out there. It is lurking in drugs and it's one that labs need to be aware of. Yeah, and it's definitely one to watch and also to think about the different sort of chain lengths you get with like protocyanazine or metocyanazine.

Absolutely, yeah, you take the nitro group off and replace it with the cyano group. You've then still got all the other modifications that you can see with nitazenes that could potentially work with this. I don't know what happens to their potency when you start doing that. I'm not sure that data is available yet.

No idea. I'm sure somebody's working on it. Okay, final paper. Let's dive in.

So this final paper looks at two fatalities as a result of sodium azide ingestion. So sodium azide ingestions are often associated with high rates of mortality. It can act to inhibit oxidative phosphorylation and produce nitric oxide, which will then lead to cardiovascular collapse and refractory shock. So this first case involves a 27-year-old male who presented to the emergency

department one hour after intentionally ingesting half a bottle of lab-grade sodium azide powder.

He was tachycardic at 121 beats per minute and had a respiration rate of 26 breaths per minute. He was also hypotensive with a blood pressure of 96 over 50. The patient was endotracheally intubated and orogastric lavage was performed 13 minutes after arrival. Blood gas results showed a pH of 7.4 with a PCO2 of 2.9 kilopascals, a bicarb of 14 millimoles per liter and a latte of 19 millimoles per liter.

They also looked at his methemoglobin level, which was 1.9% of total hemoglobin. He remained hypotensive after a crystalloid infusion and he's also given hydroxycobalamin, which can scavenge nitrous oxide. His blood pressure did improve and then he was started on hemodialysis 13 hours after ingestion with his lactate improving to 11.9 millimoles per liter. Three hours after completing dialysis, the patient experienced progressive bradycardia followed by acesusy, but regained circulation after resuscitation.

He then went on to develop pulseless ventricular tachycardia, but circulation was again regained after resuscitation. The patient was then put on methylene blue and given angiotensin II, but bedside echo revealed a severely depressed ejection fraction and he developed a worsening acidosis and anoxic brain injury and passed away 36 hours after the initial ingestion. The second case involves a 19 year old male who presented to the emergency department two hours after intentional ingestion of 40 mL of 5% sodium azide solution, which he obtained from a chemistry lab.

He was tachycardic and normotensive on admission, but became hypotensive 30 minutes later. His blood gas results showed a similar picture to the first case with a pH of 7.4, PCO2 of 1.9 kilopascals, a bicarb of nine millimoles per liter and a lactate of 12.8 millimoles per liter. Four hours after his admission, his lactate had increased to 16.5 millimoles per liter. Humodialysis was considered, but due to the time since ingestion, plasma exchange was started, which reduced the lactate to 8.3 millimoles per liter and reduced his vasopressor requirements.

However, within an hour, he developed a rapidly progressive shock and the lactate had increased to 12.8 millimoles per liter, a bedside echo revealed biventricular failure, and he then went pulseless, but spontaneous circulation was reestablished. Hydroxycobalamin was again given to treat the enhanced nitric oxide activity, but he continued to have recurring cardiac arrest and died 16 and a half hours after his initial presentation. Sodium azide is one of those compounds, isn't it? It's been around a long time used in labs, sometimes used as a preservative.

It's used in airbag fuel to produce that rapid expansion into nitrogen gas that inflates an airbag, and it's been known for a while that it is very, very toxic. Sodium azide works similar to cyanide, doesn't it? It binds to cytochrome C, inactivates metabolism at that point, stops the electron transport chain, but also it has a secondary effect in that it generates nitric oxide, and that leads to this profound vasodilation. So it's got really two modes of action.

And again, this is just two case presentations, isn't it? This isn't epidemiological data, but it is perhaps one to have on our radar. This might be a compound that people might seek out in the context of self-harm, isn't it? And people may intentionally ingest this.

And these cases show that these patients may sometimes actually present to A and E. I'm not sure how effective any treatment measures really are, are they? I'm not sure either. In this case, they clearly did best efforts.

I know that the paper they talk about the idea of inducing methemoglobinemia, which is a treatment for cyanide poisoning. I think what's complicated here is that the azide will actually also induce methemoglobinemia anyway, as part of its secondary generation of nitric oxide. So methemoglobinemia induction might not be as effective, especially if you've then got to deal with the

fact that the patient has methemoglobinemia and this profound hypotension. Treatment is best efforts, isn't it?

We do what we can to support a different hope that the patient might recover. Five very, very different compounds, all implicated in very, very different ways, ranging from household products to industrial products, to novel opioids, to venoms of creatures that normally exist in tropical waters. Showing, I think, the diversity of toxicology and showing just how much there is that can cause harm to a person. What I do think is quite interesting is that although these are all relatively new compounds, or at least their prevalence has changed significantly.

They're not new, most of these, but actually there are changing patterns in their use and exposure patterns, therefore. Actually, the mechanisms underlying them all are biochemical mechanisms that we've known about for a long, long time, aren't they? Not a lot has changed in that regard, but you still need to be aware of changes that are happening outside the lab in order to stay in touch with what's actually going on. And some of this, we still haven't got clear, solid evidence on, do we?

The hair product was an observation, and interesting. The Glasgow case of a new nitrogen analog, well, that could be the only case, and it may not necessarily have appeared anywhere else. But that's how you make progress in toxicology, isn't it? You make observations, you report them, and then that informs everybody else's view, and we keep our eye out for these things.

So I think as we go away from here, definitely, if I'm in the hair care product in the supermarket, I'm gonna be reading the label to look for glyoxilic acid. I'm probably still gonna go swimming in the Mediterranean. I'm probably not gonna let a fireworm put me off, but it is a thing that, again, to be aware of. I do hope you've enjoyed listening this week.

Do give us a like, give us a follow, and share with your friends. That'd be amazing. Hope you have an amazing week, and we'll see you next time. Bye.