English Script

Interview with Dr. Cyrus Rangan

Dr. Eyal Ben-Isaac:

Grand Rounds, an OPEN podcast.

Dr. Eyal Ben-Isaac:

Hello everyone. Today, we are here with Dr. Cyrus Rangan from Children's Hospital Los Angeles. Welcome Cy, and thank you for joining us.

Dr. Cyrus Rangan:

Thank you very much.

Dr. Eyal Ben-Isaac:

We're going to get into the topic of toxicology today. In general, what are the signs and symptoms that may be seen in children who have ingested a toxic substance or may have overdosed on a medication?

Dr. Cyrus Rangan:

Well, the signs and symptoms of a medication or drug overdose can be quite varied. You can see tachycardia. You can see bradycardia. You can see high respiratory rates, low respiratory rates, high blood pressures, and low blood pressures. I think the most important thing to think about when you're thinking about vital sign changes in children who are exposed to toxic substances, is that you usually see a relatively healthy-looking child turn into a very sick child at a very rapid rate.

Dr. Cyrus Rangan:

So when we think about infectious diseases, for example, and you think about the malaise that you may have for a day, and then the fever that may last for two to five days, and then the severe symptoms happening at day five, six or seven; that generally does not happen in most cases of toxicological exposure. You usually see a very rapid change from a healthy child to a very sick child with these vital sign changes. Also, it's

important to look for combinations of vital sign changes that sometimes work together to fall under a particular kind of category of toxin.

Dr. Cyrus Rangan:

So for example, when you see high heart rates and high respiratory rates, high blood pressures, and high temperatures all at the same time, that's an indication that the patient may have an exposure to a stimulant, like an amphetamine or cocaine or some other drug in similar classes. When you see depressed vital signs, low heart rates, low respiratory rates, perhaps even low temperatures, and maybe even low blood pressures, then you start to think of sedative drugs, hypnotic drugs, or perhaps even opiates. So combinations of these vital signs can be a clue as well.

Dr. Eyal Ben-Isaac:

So basically we should not be fooled by a well-appearing child who comes into our office or the ER who we think may have had an ingestion because they can turn on us.

Dr. Cyrus Rangan:

That's very true. When we sometimes hear about children who come into the medical setting and they were possibly exposed to a drug, let's say a half an hour ago, that's a child who may continue to look relatively well while they're in the office. And then it may be at hour two or hour three that you start to see some major changes. This is one of the reasons that we almost universally advise with my colleagues at Poison Control that when you get young children who come in with possible ingestions, even if you're not sure what they may have taken, that we usually have a four to six to possibly even eight-hour window of observation of that exposure to ensure that severe signs don't develop.

Dr. Eyal Ben-Isaac:

Really important points. Thank you. There are certain signs and symptoms we often see with ingestion, such as vomiting, changes in mental status, heart rate changes, like you mentioned earlier. But are there any subtle differences that exist between children and adults that we should be aware of?

Dr. Cyrus Rangan:

One thing that is interesting about most things in toxicology is that the vast majority of time, the kinds of symptoms that you see in adults are the kinds of symptoms that you tend to see in children. Now, the big differences, of course, are going to be in dose. So with children, when you're talking about a young child who obviously weighs less than

an adult, then it takes much less of a dose to cause the same symptom to occur. In fact, there are a number of adult dosage medications out there where we consider one swallow or one bite or one pill exposure to those particular medications to be potentially fatal to a, let's say, less than two-year-old child.

Dr. Cyrus Rangan:

So this applies, in particular, when we're talking about blood pressure medications or some antipsychotic medications or hypoglycemic medications. These are the kinds of medications where one adult dose of those medications potentially could be fatal in that young child even though, again, they may look good in the early going. They can change on you quite significantly later on. So dose is probably the biggest difference that you see in children versus adults.

Dr. Cyrus Rangan:

The other issues that we tend to see is that when children encounter a lot of these toxins, they tend to encounter them on an accidental basis. So in other words, when they take these, when they are exposed to these medications or whatever substance they may have been exposed to, they don't tend to intentionally take a number of pills, although we do see that some children who are a little bit too curious may take a whole bottle of pills because it happens to taste good. But usually it's not intentional in terms of causing intentional harm. Whereas in some of our older children who are teenagers, those are the situations where we may see intentional harm and perhaps suicidal intent with their overdoses. Those are situations where we may see sometimes even massive overdoses that can be extraordinarily severe.

Dr. Eyal Ben-Isaac:

Absolutely scary that one pill can just change everything for a little child. So thank you for informing us of that. Let's try to play an educational game here. We're going to try to discuss some possibly nonspecific presentations in pediatrics, and maybe you can point out when we should think about an ingestion and which ingestion. So I'll give you a bunch of cases and you can go from there. How about a three-year-old with persistent vomiting for one day?

Dr. Cyrus Rangan:

Okay. So just about any ingestion, no matter whether it's a toxic ingestion or even a nontoxic ingestion, is capable of causing abdominal discomfort and vomiting in almost any patient, no matter the age. So when we think about patients who may have persistent vomiting throughout the day, then we have to start to think about whether the

ingestion itself has caused some form of damage within the gastrointestinal tract or perhaps the upper respiratory tract. So here we start to think about caustic ingestions, so ingestions of acid, types of compounds, or base compounds that may be causing injury to the mucosal layer, or perhaps even deeper than the mucosa and that results in irritation that then results in excessive vomiting.

Dr. Cyrus Rangan:

Other situations where you may see excessive vomiting are when you have an absorption of a toxin that then causes other systemic effects that lead to vomiting. So for example, if you ingest a toxin that causes liver injury, well, it's that liver injury that could then result in vomiting. So it may not be a direct gastrointestinal effect, but it may be a manifestation of severe disease that's going on in some other organ system. When it comes to the caustic ingestions, the most important thing to do, of course, is to make sure that there is no further exposure.

Dr. Cyrus Rangan:

If there is continued presence of the material on the face, for example, of course, wash the face. Wash the outside of the mouth and hands as well. Because if the child got it on their hands and they're continuing to put their hands in their mouth, that may be another source of that exposure. So to make sure that all the external sources are no longer causing a threat. After that, it tends to be a very, very strict observation. That is probably the number one most important thing to do is to actually stand back from a lot of these children and observe. Sometimes there is a tendency in cases of possible poisonous exposures to try to do too much.

Dr. Cyrus Rangan:

These are cases where standing back and observing and just simply watching the situation play out can actually be more helpful than some of the interventions that we've done in the past. For example, you don't want to necessarily rush to intubate patients like this because you may even cause more injury by the instrumentation of the intubation equipment. So making sure that the child remains calm, making sure that the respiratory status is reasonable enough so that the child can maintain reasonable respirations, whether it's rate or quality of respirations, and making sure that that the child doesn't become agitated. Because the more excitement that that child has, the more likely that they will cause breathing problems to actually occur in the face of these kinds of injuries.

Dr. Cyrus Rangan:

Vomiting, but also coughing and drooling because of upper respiratory injury, if children have any of those symptoms, those are virtually automatic admissions for inpatient hospitalization and close observation, perhaps even to an intensive care unit if there is potential respiratory compromise. One thing that we probably say the most in these cases in terms of what not to do, is to do a blanket dosage of steroids. There may be situations where steroids can be appropriate in certain situations of caustic injury. It's rare that we ever actually do it.

Dr. Cyrus Rangan:

In fact, most of the medical literature out there says that when you do give steroids to patients like this, we tend to make the situation worse. It actually increases the risk of bleeding and other complications as well. So that's probably the one area where we actually caution hospitals against giving an interventional dose of steroids.

Dr. Eyal Ben-Isaac:

Thank you for including the criteria or what to look for when considering admission because those are all important points. All right. Let's go to a four-year-old found to be hypoglycemic.

Dr. Cyrus Rangan:

Hypoglycemia can happen from a number of different toxins as well. As you can imagine, the most obvious reason why a child is hypoglycemic is because they took a medication that is for the purpose of hypoglycemia, in other words, oral diabetic medication that perhaps belongs to an adult in the home. This falls into the category of one of those that I talked about before where perhaps one pill could kill a small child, let's say, less than two years old. So if we're talking about a medication like glyburide or glipizide, which are sulfonylurea medications that are for oral treatment of diabetes in adults, these are medications that specifically go to the pancreas and tell the pancreas to secrete as much insulin as possible so that blood sugar levels can be brought down when diabetic patients have too much in their blood.

Dr. Cyrus Rangan:

However, when a young child takes it who's normoglycemic, well, you can really, really throttle those levels down quite significantly. We've seen children who present with blood glucose levels of 10, 15, 20, in that range sometimes within, let's say, about three hours after overdose. So that can occur with the oral hypoglycemics. One caveat about the oral hypoglycemics is that, remember, these are drugs that are generally designed to be taken maybe once in the morning and last throughout the day for the adult who's

taking that medicine. So you may not see the peak of the effect or even the onset of the effect in a young child until much, much later.

Dr. Cyrus Rangan:

We've seen many cases where the first time that that child becomes hypoglycemic is maybe 12 to 18 hours after the initial exposure. So whenever we see very young children, again, let's say a child who's less than two years old, these are children that are virtually automatic admissions for one pill exposure to these hypoglycemic so that we can continue to check their blood glucose and observe them usually overnight to make sure that they're not developing hypoglycemia. Because they can look very, very well for maybe that first 12 hours or 18 hours, and then suddenly have an issue with hypoglycemia.

Dr. Cyrus Rangan:

The oral hypoglycemics are one of the most important and severe reasons why a child is hypoglycemic, but there are a number of other medications that can cause hypoglycemia as a side effect for a number of other problems that they may cause. One of the more important ones is beta-blocking antihypertensive medications, so medications like propranolol, metoprolol, atenolol. All of these beta-blocking medications have the capability of causing hypoglycemia because of their interaction with G proteins and the way that we break down glycogen.

Dr. Cyrus Rangan:

They also have some effect on the pancreas as well. So there are actually four or five different mechanisms involved, metabolically speaking, as to why hypoglycemia occurs. But these patients can come in with very, very low sugars and sometimes less than 50. Even though you may be concentrating on the fact that this child has a very low blood pressure because of this medication that they took, they also may have accompanying hypoglycemia as well. Another one that can cause hypoglycemia too that's very important, and we'll be talking about this a little bit later hopefully, is aspirin.

Dr. Cyrus Rangan:

Salicylates are notorious for causing problems with blood glucose. In fact, with salicylates you can actually get hyperglycemia or hypoglycemia, depending on the situation. So a number of medications can cause that. Primarily, the way to treat it, of course, is to rescue the patient with a glucose infusion, usually a bolus infusion. With the oral hypoglycemics however, one thing that we do first-line with these patients is to give them octreotide. The octreotide essentially helps to sort of wrap a net around the

issues with the pancreas to tell the pancreas to kind of flip the off switch to cool it on the insulin secretion.

Dr. Cyrus Rangan:

That helps you get ahead of the game a little bit, because one thing that can happen with oral hypoglycemics is that you give a lot of glucose and then you put the patient, let's say, on a glucose infusion. That glucose infusion also goes to the pancreas and tells the pancreas to please secrete more insulin, and you've already got a drug onboard that's telling the pancreas to secrete a lot of insulin. So you could be chasing your tail when you give a lot of sugar to patients who've taken oral hypoglycemics as a toxic exposure.

Dr. Cyrus Rangan:

So we give octreotide these days sometimes as the first line to try to tell the pancreas to calm down. And then we keep the patients without a continuous glucose infusion. We continue to check their blood glucoses, and we give bolus doses of glucose as needed if they happen to drift down. Usually those patients will get better in about 24 hours or so.

Dr. Eyal Ben-Isaac:

Great review of all the potential medications that can cause hypoglycemia. And again, I think you're telling us observation, observation, observation in many of these kids.

Dr. Cyrus Rangan:

Very true, very true.

Dr. Eyal Ben-Isaac:

All right. How about an eight-year-old with jaundice?

Dr. Cyrus Rangan:

Jaundice can occur, of course, in any patient who's got some form of liver injury. When we think about the kinds of things that cause liver injury in toxicology, there are a number of them. You may get liver injury as a consequence of other systemic issues like, for example, if you have a patient who has taken a very severe overdose of amphetamines or some other stimulant. Well, those patients can end up with what we sometimes call shock liver because of issues of liver perfusion that may occur as a

result of their sympathomimetic or stimulant overdose. So we can get sometimes liver injury because of those kinds of issues and that, of course, could lead to jaundice.

Dr. Cyrus Rangan:

But when we think about things that can cause direct injury to the liver, there are a few out there that are very important to understand, the first of which is acetaminophen. Acetaminophen is probably the most common reason for toxic liver injury right after alcohol, worldwide. When we talk about acute exposures, acetaminophen is actually number one. When acetaminophen causes liver injury, however, it does take a little bit of time and actually a lot more time than we're used to in toxicology.

Dr. Cyrus Rangan:

When a patient comes in even with a very severe overdose of acetaminophen, let's say you had a patient take a full bottle, you're not going to see those liver injury effects sometimes for several hours and possibly even a whole day after they take that overdose. This is probably the number one reason why we check acetaminophen levels in so many cases of patients who present with any kind of toxicological overdose to the medical setting. So even though the patient may not necessarily admit to have taken acetaminophen or perhaps even denied taking acetaminophen, we still check acetaminophen in the vast majority of cases that present to the hospital.

Dr. Cyrus Rangan:

Why? Because the effects tend to occur several hours later or perhaps even the next day, but the elevated level in the blood will occur early. We can wrap a net around that and start treating that early on when we see those elevations. When acetaminophen causes injury to the liver, it tends to cause an injury that is what we call indirect. In other words, it's not the acetaminophen that's toxic to the liver. It's a product that acetaminophen gets metabolized into. That's what actually causes the injury.

Dr. Cyrus Rangan:

So when acetaminophen enters the liver, it enters in the portal triad. And then as the acetaminophen moves towards the central vein in the hepatocyte, that's when it starts causing the injury. Most of the injuries around the central vein, that's what we call centrilobular hepatic necrosis. Even though a lot of the liver can be injured quite significantly from acetaminophen poisoning, we must remember, of course, that all of the regenerative cells in the liver tend to be around the portal triad area. So even though you can get a lot of damage around the central vein, the cells around the portal triad area tend to be relatively intact.

Dr. Cyrus Rangan:

So patients with acetaminophen poisoning, even though their AST and their ALT or transaminases may be in the several thousand range, these patients tend to recover relatively well with treatment for acetaminophen poisoning, which is N-acetylcysteine. But these patients, of course, can develop jaundice after that liver injury does occur and it may take several days in order for it to return. Another one, of course, it can cause liver injury in the same kind of scenario is iron poisoning. Hopefully, we'll be able to talk about iron poisoning a little bit later as well.

Dr. Cyrus Rangan:

But iron poisoning is one that causes direct hepatic injury. It's a little bit of a different story and different kinds of pathophysiology than acetaminophen, but that's something that can cause direct liver injury and lead to jaundice, of course.

Dr. Eyal Ben-Isaac:

That was a great review of acetaminophen poisoning and ingestion. That was one thing that we see a lot of, and it's really hard to take care of. So thank you. All right. Let's move to the heart, 15-year-old with palpitations.

Dr. Cyrus Rangan:

Okay. So palpitations, now, when we think about palpitations, really anything could be happening with the heart. You can have palpitations with high heart rates. You can have palpitations with normal heart rates. So palpitations really just fall into the general category of dysrhythmias. When we think about drugs that can cause dysrhythmias, again, we're talking about a very enormous spectrum of drugs out there that can do this. When it comes to drugs of abuse, probably cocaine is one of the most notorious for causing abnormal heart rhythms along with tachycardia.

Dr. Cyrus Rangan:

Cocaine is one of the most notorious for causing those kinds of problems. Virtually any stimulant drug, like amphetamines, of course, can also cause palpitations. Usually you won't see vasoconstriction and myocardial infarction like you see with cocaine, but amphetamines and related drugs can give you high heart rates, sinus tachycardia, sometimes more severe manifestations like ventricular tachycardia have been noted to occur as well. When it comes to prescription medications, the tricyclic antidepressants and phenothiazine drugs, both are notorious for causing dysrhythmias, so those are drugs that we need to be cognizant of.

Dr. Cyrus Rangan:

When it comes to tachycardic types of dysrhythmias, those are the general classes of drugs that we tend to think of. But there are a number of drugs that can actually cause bradycardia, but then perhaps later on lead to dysrhythmias that then manifest as palpitations. This is notorious in the category of digitalis drugs or cardiac glycoside drugs. You can get almost any kind of dysrhythmia as a result of the digitalis exposure, except for a rapid ventricular response from atrial tachycardia. Obviously, because of that slowing of the AV note, you won't get that. That's probably the only dysrhythmia you can't get. Every other dysrhythmia is on the table. So cardiac glycosides are an important cause of those kinds of cardiac manifestations as well.

Dr. Eyal Ben-Isaac:

So with that, maybe we can next review the presentation of some of the other common ingestions that we see out there, such as iron, aspirin, any other over-the-counter medications you may want to cover as well.

Dr. Cyrus Rangan:

Sure. Well, let's start with aspirin in this case, because we don't have aspirin in households as much anymore because of the advent of acetaminophen several decades ago. That has basically replaced aspirin as the anti-fever medication. So we don't see as much aspirin as we used to. But when it comes down to severe manifestations from over-the-counters, aspirin is still near the top of the list in terms of causing severe problems when it is the medication that the child perhaps overdosed on. Now, in terms of what you can see with aspirin poisoning, aspirin is a very interesting drug in that it essentially causes a multi-system kind of presentation.

Dr. Cyrus Rangan:

When children overdose on aspirin, you can get mild symptoms that may include maybe some difficulty hearing because of the tinnitus that aspirin can cause, maybe a little bit of nausea and vomiting. Maybe that's it. That can be the mild presentation of aspirin poisoning. But as more and more aspirin is ingested, you can start to get moderate and severe manifestations that include many organ systems. As I mentioned, from the ear, nose, and throat standpoint, you can get tinnitus. From the respiratory standpoint, you can get sometimes noncardiogenic pulmonary edema.

Dr. Cyrus Rangan:

That is a very, very severe manifestation and it's quite rare. It doesn't really occur in young children. It is something we tend to see more in older teens and adults. In fact, I

don't think it's ever been reported in anybody less than 16 years old. But it's something to think about when you think about the respiratory issues of aspirin. From a metabolic standpoint, aspirin can cause a number of metabolic derangements, in particular with your acid-base status. Normally, of course, our blood pH should be at a stable 7.4. But when aspirin is ingested, you can have a number of pathological processes that can pull on that 7.4 high or low, depending on the phase of poisoning that you're in.

Dr. Cyrus Rangan:

One thing that aspirin does is it goes to the respiratory center in the brain and it basically tells you to start breathing more deeply and sometimes more quickly. So because of the hyperpnea and tachypnea, you can then get a respiratory alkalosis and that will pull your pH above 7.4. But in addition to that, aspirin likes to go to your tissues and it likes to shut down aerobic respiration and convert you to anaerobic respiration. As a result of that, you get some metabolic acidosis. So now you've got a respiratory alkalosis and a metabolic acidosis competing with each other. These are two primary processes.

Dr. Cyrus Rangan;

It's not compensation. It's two primary processes. So you can have one process pulling the pH above 7.4 and another one trying to pull the pH below 7.4. Why is this important? Because when patients present with aspirin poisoning and we get their serum pH with a blood gas and we see a 7.4, well, that may not necessarily tell you that the patient is perfectly fine and healthy. So with aspirin poisoning, probably the most important pearl to remember is don't regard the pH by itself as the way of assessing how healthy the patient is. You've got to look at the patient.

Dr. Cyrus Rangan:

If there's any take-home point, it's the same thing, of course, that we tell our medical students and our medical residents all the time, look at the patient, look at the patient, look at the patient. How the patient looks is so much more important in aspirin poisoning than your labs, which sometimes can be a little bit misleading. Another thing to remember about aspirin poisoning is that not only does it cause these derangements in acid-base balance, but it also causes you to lose a lot of potassium generally at the level of the kidneys.

Dr. Cyrus Rangan:

That can be one of the things that some people forget to monitor because you're looking at so many other severe issues that occur with aspirin poisoning and sometimes the

potassium issue gets a little bit left to the side. We have seen situations where the potassiums will drift down very significantly to, let's say, 2.0. These are situations, of course, where patients now may have dysrhythmias as a result of their aspirin intoxication. So that's something that we have to always make sure that we're aware of as we're treating these patients.

Dr. Cyrus Rangan;

As far as the treatment of these patients is concerned, we give these patients a lot of sodium bicarbonate. Now, again, not all cases are going to need a lot of sodium bicarbonate. Mild cases generally are treated with observation and IV fluids. Moderate to severe cases may require sodium bicarbonate in order to try to correct the acid-base imbalance that is going on. So in terms of what to do about this, as I mentioned, we give a lot of sodium bicarbonate because we want those patients to maintain their pH above 7.4. In fact, we want to get them to around maybe 7.45.

Dr. Cyrus Rangan:

So that's the most important thing about aspirin is keeping that pH above 7.4 while you're treating that patient and watching that potassium. If you're doing just those two things with aspirin poisoning, you're going to do your patient a lot of good. About 90% of your treatment is right there with those two particular issues. Most aspirin poisoning patients tend to get better within about 24 hours or so. In general, those treatments will work if you have a very severe overdose or if you have a patient perhaps who presented very late after their overdose, they may have extremely severe manifestations that don't respond to those treatments.

Dr. Cyrus Rangan:

In those cases, we move on to hemodialysis as the way to get rid of that aspirin and to try to correct their pH balance and try to get their clinical picture under control.

Dr. Eyal Ben-Isaac:

Any other adjustments you want to go over, iron, for example, because that's a big one, or any over-the-counter medications, cough and cold preparations.

Dr. Cyrus Rangan:

Sure. Iron is a good one to go over as well. When it comes down to the single most common reason why a child may die from a medication overdose in the United States at least, it is actually still iron poisoning. Now, it's not that many deaths. It's maybe about three to six deaths per year. But in terms of single medications that cause the most

deaths, iron is still at the top of that list. Now, we used to see a lot more iron intoxication in the past than we do these days. Child-resistant packaging is one of the reasons that we have seen a sharp decline in the past several decades with iron overdose.

Dr. Cyrus Rangan:

But we have seen situations where very, very high-dose iron pills are in homes. One of the reasons that that may occur is if you have a mom in the home who was recently pregnant, who was taking their high-dose iron for pregnancy and perhaps has a lot of that medication leftover and is still in the home. I'm just going to state this from a human behavior standpoint. It's possible and it does happen that perhaps that mom was prescribed these iron pills in a very secure, what we call strip packaging, where the iron is in individual packages in a strip and needs to be removed in order to access it.

Dr. Cyrus Rangan:

Well, again, from a human behavior standpoint, that can be a difficult thing, especially in a daily medication regimen for people to have to break into those single strip packagings every single day to take their iron. A lot of people go ahead and take them all out and then put them into a bottle so that they're easier to take on an everyday basis. It's not something we ever encourage people to do. It's not something that certainly the FDA or any other organization would ever encourage anyone to do, but it does happen. Because it does happen, that means that there are situations like this where children have easier access to iron than they would otherwise if those pills remained in those strip packages.

Dr. Cyrus Rangan:

Now, when children get into iron, it's interesting. When you talked earlier about sometimes the differences between pediatric and adult poisonings, here's one situation where you do see an interesting difference. Normally, when we think about iron poisoning, children get or patients tend to have what we call phase one of that poisoning, which tends to include a lot of abdominal issues, including vomiting and bloody diarrhea. The reason you get bloody diarrhea is that iron is a corrosive metal. So it causes corrosion to the mucosal layer in the gastrointestinal tract and you get bleeding.

Dr. Cyrus Rangan:

However, what's interesting is that that phenomenon tends to be observed a lot more in adults. When it comes to young children, there have been many cases of severe systemic iron poisoning where children don't develop any bloody diarrhea and, in fact,

may not develop severe gastrointestinal symptoms at all. We don't know necessarily why that occurs, but it does occur. So just because a child presents with iron exposure, and if that child doesn't really have any gastrointestinal symptoms, it's still possible that that child may develop severe iron poisoning as a result of absorption of that iron.

Dr. Cyrus Rangan:

So keep that in mind that that phase one sometimes it can be very mild in very young children. Now, iron then moves on to what we call phase two of iron poisoning. Now, phase two of iron poisoning is what we call the latent phase. Why is it called a latent phase? Because during that phase two, you tend to see a patient who looks relatively well. The reason that these patients look relatively well is that they will come in with those gastrointestinal manifestations, essentially looking like a patient who had a viral gastroenteritis. They have vomiting, maybe some loose stools and they lose some water.

Dr. Cyrus Rangan:

And then we give them intravenous fluids or oral challenges that then bring their hydration status back up to normal. That's why these patients look good in this so-called phase two of iron poisoning when they look relatively well, the latent phase. But if patients never were treated with those IV fluids, let's suppose you had a late presenter, well, you may not see that phase two. So the reason we have phase two is that it, in fact, is iatrogenic. We cause phase two to happen because of the fluids that we give these patients.

Dr. Cyrus Rangan:

Phase three of iron poisoning involves the systemic absorption of the iron that is the now going into your tissues causing organ damage or organ injury. There are a few places in the body that are notorious for picking up iron and causing a lot of problems, but iron can be toxic to virtually any organ in the body. But the places where we worry about the most are the heart and the liver. So we've seen hearts that just simply stop working because of that manifestation of iron.

Dr. Cyrus Rangan:

We've seen livers that start to get directly injured by the corrosive nature of the iron and also have this issue where their cellular respiration gets impeded. So our liver's ability to regenerate after iron overdose injury is much more impaired than it is with, let's say, acetaminophen overdose. These are patients that may need to be considered for liver transplant relatively early speaking, when they start to get injury from iron overdose.

Dr. Cyrus Rangan:

We will give additional medication in the form of deferoxamine. What is doing the most work is your careful observation and your symptomatic care. That is probably doing 90% of the work, whereas the deferoxamine is probably doing maybe 10% of the work. But in severe overdoses, it is a very necessary drug and something that we do need in order to try to bring those levels down as quickly as possible and avoid a bad outcome.

Dr. Eyal Ben-Isaac:

Thank you again, Cy. This was incredibly informative and very educational. I always learn more and more each time I hear you speak. Are there any specific takeaway points that you would want our audience to keep in mind?

Dr. Cyrus Rangan:

Well, I think one thing that you brought up earlier is the notion of observation., There's that old adage, if you see a crime occurring, it's don't just stand there, do something. Well, it's actually somewhat the opposite when we think about toxicology. In fact, we sometimes very colloquially say in toxicology, don't do something, just stand there. So it's a little bit of the opposite of our instinct sometimes.

Dr. Cyrus Rangan:

What I mean by that is that sometimes we do feel compelled to do too much to intervene with instrumentation, to try to remove medication, or to try to get overly aggressive with the use of antidotes or other measures to try to counteract or neutralize a poison when, in fact, the vast majority of our treatment of almost any kind of toxin is good old-fashioned observation and careful treatment of symptomatic issues that occur in these patients and monitoring of vital signs, monitoring hydration status, and monitoring mental status.

Dr. Cyrus Rangan:

If you do those things in toxicology, most of your patients will get better. Sometimes the interventions that we have can do more harm than good. So I think that's one of the most important take-home points about toxicology when it comes to children or adults is to make sure that we take a very measured approach to what we're doing to these patients and that we have a good reason for applying the therapies that we are considering.

Dr. Cyrus Rangan:

Probably the second most important thing I would say is important to keep in mind is that when you have patients who come into your medical setting who, again, were looking really good and now don't look good and it's a relatively short period of time in between those two phases, those are the kinds of patients where we should be thinking that there could have been a toxicological exposure. So many other disease processes that we're familiar with in pediatrics tend to take a few days to develop, especially in infectious disease.

Dr. Cyrus Rangan:

But with toxicological exposures, things tend to happen relatively quickly. So when you have that child who comes in and the parent says, "They were looking just fine several hours ago, and now they look like this," those are the kinds of situations where we should be considering the full toxicological differential, even though it may not necessarily be the diagnosis for that patient.

Dr. Eyal Ben-Isaac:

Thank you, Cy, for educating all of us today. This was really great.

Dr. Cyrus Rangan:

You're welcome. My pleasure.

Dr. Eyal Ben-Isaac:

I hope you enjoyed my conversation with Dr. Rangan as much as I did. If you'd like to hear more pediatric experts, subscribe wherever you listen to podcasts and keep in touch with us by subscribing to learnwithopen.org and check out the links and resources in our show notes. If you liked what you heard, please rate us and leave a review. This podcast is produced by the Online Pediatric Educational Network and Mindy Lee. This episode was mixed and edited by Daniel Lev. Our music was created by Daniel Lev and Juan Espinoza.