



American Society of
Anesthesiologists[™]

Central Line
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VOICE OVER:

Welcome to ASA's Central Line, the official podcast series of the American Society of Anesthesiologists, edited by Dr. Adam Striker.

DR. ADAM STRIKER:

Welcome back to Central Line. I'm Dr. Adam Striker, your host and editor. Today, I'm here with Dr. Russell McCallister, a member of the Anesthesia Continuing Education, or ACE editorial Board and professor and chair of anesthesiology for Baylor College of Medicine in Temple, Texas. As many of you know, we occasionally tackle a topic from the current ACE issue. And today we noticed an interesting item that Dr. McCallister wrote for the latest issue of ACE. So we invited him on to discuss the dangers and treatment of sarin. So, Dr. McCallister, thanks for joining us today.

DR. RUSSELL MCALLISTER:

Thank you. Appreciate you having me on.

DR. STRIKER:

Love to have you. And I'm looking forward to talking about this because this is not a typical topic we cover on Central Line. But before we get to the specific topic, do you mind telling us a little bit about yourself and how you got involved with the ACE program?

DR. MCALLISTER:

Sure. I've been at Baylor, Scott and White in Temple, Texas for 28 years and I'm currently the chair of anesthesiology there. Just recently formed an affiliation with Baylor College of Medicine. Our campus has a branch campus of the Baylor College of Medicine here. So looking forward to that new affiliation.

DR. STRIKER:

And how did you get involved in the ACE program?

DR. MCALLISTER:

So I enjoy writing and I was initially considering helping write for American Board of Anesthesiology and had an interest in that. But in the interval time, I was a frequent user of ACE and I saw that the ASA was asking for committee assignments and I saw that that was one of the options. And so I reached out and applied for that and was very happy to get a call. And they actually called me and said, Now you realize this is a very large time commitment. Are you willing to travel to Chicago and meet four times a year? I stated that I was and it's a very time-consuming job, but one that I enjoy. And I've met a lot of outstanding people on the editorial board, so I've enjoyed my time there.

DR. STRIKER:

Wonderful. Well, let's talk about the organophosphate pesticides broadly and then we can talk about specifically sarin. But let's put it in context for the listeners, the importance of the topic, why we should be concerned and know about this.

DR. MCALLISTER:

Sure. So organophosphates are typically what we see in pesticides used in the agricultural industry. And reportedly there's as many as 3 million exposure cases per year worldwide and up to thousands of deaths due to organophosphate poisoning. Sarin is an organophosphate poison, but it's obviously not used as a pesticide, but the physiology is very similar.

DR. STRIKER:

Give us a little bit of history on the development of organophosphates. Where did they come about when were they used most frequently?

DR. MCALLISTER:

Sure. So sarin specifically was developed in 1938, and it was originally to be used as a pesticide, but they quickly found out that it was very potent and dangerous. So they decided that it was not safe to use as a pesticide. But then it was developed as chemical warfare agent.

DR. STRIKER:

When were they first used as a chemical warfare agent and how has that progressed over time?

DR. MCALLISTER:

Well, these agents are actually banned by the 1925 Geneva Protocol. There are multiple instances in modern history where these nerve gas agents have been used in attacks or assassinations. Most notably, there was an attack on a subway in Tokyo back in 1995, and that led to over 600 people requiring hospital treatment. And then there's reports of cults that have used these agents to kill dissenting members back in the mid 90s. And then it's been used by governments in the Middle East as agents against their own civilians that were rebelling.

DR. STRIKER:

We often learn about, in medical school or in anesthesiology residency, sarin and VX together in the organophosphate category. Briefly, what is the difference between sarin and VXs?

DR. MCALLISTER:

Well, VXs is far more potent and volatile than than sarin. So it's in even tiny amounts. it's it's far more deadly. But sarin and VXs are both very dangerous.

DR. STRIKER:

Well, let's bring it back to anesthesiology. Why should practicing anesthesiologists care about chemicals that are used as warfare agents? And why do we need to know this this knowledge?

DR. MCALLISTER:

I think it's interesting because in most hospitals, anesthesiologists are key members of the response teams for mass casualties and disasters. So most of these situations involve the need for airway management, and that's why anesthesiologists are on those teams. This is an attack of nerve gas, such as sarin or VX, one of the main components of treatment of the patient is airway management. So it's very likely if you do live somewhere that there's an attack that occurs and the victims are brought to your hospital, the chances of them requiring airway management are very high. So I think it's important for us to understand the possibilities. And as the ACE editors always like to

say, have a walking around knowledge of why this may be important. And it may be that we go through our entire career without encountering such a thing. But in the event that something does occur, having at least a baseline understanding of the important aspects of it, I think is very useful.

DR. STRIKER:

Is an anesthesiologist more likely to encounter it in a mass casualty form or with a patient who's had exposure to a pesticide when it, not necessarily sarin specifically, but organophosphates in general?

DR. MCALLISTER:

Yeah, I think organophosphates are used far more widely. So the chances that you're going to encounter one of those patients when you're consulted to assist with airway management in the emergency department are far more likely. But because the typical insecticides organophosphate agents are not nearly as deadly, I think we typically would have more time to respond and prepare and take care of the patient. And also the chances of exposure of the health care team is a lot lower with the insecticide organophosphates as opposed to the nerve agents such as sarin or VX where contamination of the health care team is a real possibility.

DR. STRIKER:

Okay. Well, let's turn to sarin gas, specifically the topic of the ACE question. Why don't you give our listeners a little bit of basic science background. Let's talk about the mechanism of action of sarin and any pertinent details about the chemistry that you'd like us to know.

DR. MCALLISTER:

Sure. So as we talked about before, it's a very potent and dangerous gas. It's essentially odorless, clear and colorless. And so sometimes people can get exposed and not realize it until they're in trouble. So sarin is an organophosphate agent and has a lot of similarities to other organophosphates, as we mentioned, such as the insecticides. But the key difference with sarin and VX is that they're fluorinated and therefore that makes them much more volatile and potent than the typical insecticides. And then on the physiologic level, as you probably recall from physiology and pharmacology, organophosphates are acetylcholinesterase inhibitors. And what that means is that acetylcholine released into the neuromuscular junction will accumulate

there and that results in effects that are basically equivalent to continuous stimulation of those cholinergic nerve fibers.

DR. STRIKER:

Give us a little bit of background on the cholinesterase agents that might be encountered now as opposed to, let's say, prior to World War Two?

DR. MCALLISTER:

Sure. So as you know, we've we've got anticholinesterase agents in our pharmacy at our hospitals. That includes our typical agents such as Physostigmine, which was one of the first anticholinesterase agents that were discovered. And we still frequently use Neostigmine as a reversal agent for our neuromuscular blocking drugs. The key difference here is that when the organophosphate compounds were developed, they're classified in the literature as an irreversible type of drug, which means that they're going to produce symptoms for a far longer duration of time than our reversible agents that we typically use pharmacologically.

DR. STRIKER:

Before we get into the treatment, let's talk about how the typical exposure to sarin would manifest. What forms does the the chemical take and how are people most vulnerable to it?

DR. MCALLISTER:

Right. So it can be a powder or it can be vaporized and in the air. So the different ways that you can be exposed to it include the skin and the symptoms develop especially rapidly when when you have eye contact or if the agent is inhaled. But you can also ingest it through contaminated food or liquids. So if the exposure is through inhalation or with contact with the eyes, the symptoms typically appear within seconds. Whereas if the exposure is through contaminated foods or liquids, then it can take several minutes or possibly even an hour or so before the symptoms arise.

DR. STRIKER:

If I'm not mistaken, wasn't sarin or VX in the news when it came to an assassination attempt involving North Korea. Is that right?

DR. MCALLISTER:

Yes. During my research for this ACE question, I found it really interesting some of the ways that this has been used in the news. So Kim Jong Nam is the half-brother of Kim Jong Un, who's the leader of North Korea. So in 2017, Kim Jong Nam was at a Malaysian airport and was in a crowd, and two separate women approached him and brushed their hands against his face in succession. And he immediately began to show symptoms of distress. And the team that was with him treated him rapidly and emergently. However, in a short period of time, he decompensated, had respiratory distress, and eventually passed away there at the airport before they could even get him to the hospital. And interestingly, each of the women involved in the attack survived. And that led to a lot of confusion about what exactly happened. I found it very interesting, as a former chemistry major, I found it both horrifying and fascinating all at the same time. But VX is the potent agent that was used in this attack and it's what's called a binary compound. And what that means is it's made when two or more stable and non-toxic chemicals are mixed together and suddenly you get a very toxic reaction that leads to a very dangerous and volatile compound. So in this case, each of the women that was approaching the victim had one of the chemicals on their hand, and these were each nontoxic precursor liquids and each one in succession deposited that liquid onto the victim's face. And when that second chemical was deposited onto the victim's face, then it led to a chemical reaction, producing the deadly gas. And that's what led to Kim Jong Nam's death. I had not heard that story in the news or that version of it in that much detail. So I found that very interesting. That VX is actually a binary agent and learning about what all that entailed was very interesting.

DR. STRIKER:

That is interesting. I had not heard that, but I think you stated it well. That is it is incredibly scary. I mean, it is fascinating from a chemical standpoint, but as you stated, horrifying nonetheless. Well, let's talk about symptoms of sarin exposure. What should we be looking for?

DR. MCALLISTER:

So I think we all remember from physiology and pharmacology hearing about cholinergic crisis. Any time we have a patient that's exposed to one of these dangerous gases, the severity of the symptoms is going to depend on the volume and the duration of the exposure. Because of sarin's potency, even small amounts can result in the typical symptoms that we recall from pharmacology that make up the cholinergic crisis. The most pertinent to our interests include salivation, lacrimation, diaphoresis, bronchospasm, diarrhea, muscle weakness, or sometimes even paralysis. And then also typically they can get severely bradycardic. And these symptoms appear within

seconds. And so we've got to be ready to to recognize them and and be ready to treat them.

DR. STRIKER:

We'll want to discuss treatment, various methods for managing Syrian exposure. But let's first take a short break, so please stay with me.

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Your patients depend on you. And you can depend on GE Healthcare for our trusted legacy of industry leading anesthesia care solutions. Take advantage of one integrated platform for insightful decisions and individualized care to help you stay one step ahead of critical moments for your patients. With our latest innovation, you can quickly achieve and maintain the end tidal oxygen and anesthetic agent targets you set made possible by the only FDA approved device indicated for patients 18 years of age and older, bringing automation to the US anesthesia community.

DR. STRIKER:

Okay. Well, we're back with Dr. Russell McAlister from Baylor College of Medicine in Temple, Texas, talking to us about one of the questions on the new ACE issue involving sarin gas. And we've already discussed some of the chemistry of the gas and the effects that it can have on patients. So let's turn to treatment now. I remember from medical school, years ago, the thing that was hammered into our heads when it came to organophosphate poisoning was atropine and tupa. Atropine and tupa. I imagine realities may be a little more nuanced than that. And there's probably more we can offer. So do you mind telling our listeners a little bit about the treatment for for sarin exposure?

DR. MCALLISTER:

Sure. So atropine and tupa, that has not changed. Those two are very important. But a couple of other things to note. There's multiple considerations when one of these patients arrives to our hospital. The first action needs to be to diminish the ongoing exposure. So depending on the type of exposure that they have, if the agent is in their clothing, they can be having ongoing exposure. So one of the earliest things that needs to be done is to remove the clothing and place it in a sealed bag to prevent exposure of our healthcare team. Following that, it's important to remember that very dilute

hypochlorite bleach solution is really effective at denaturing these compounds and then this should be followed quickly with rinsing them off with soap and water. So getting the agents off of the patient is a key first step if time allows. And so that's important. Another thing I found very interesting is that sarin is heavier than air and in large attacks it will settle in low lying areas. So if this initial cleansing is occurring outside, that's safer. Even better is if it's not in a low lying area. So getting to higher ground, if that's feasible at your facility, is beneficial.

DR. STRIKER:

And let's talk about the chemistry behind the antidotes, atropine and 2-PAM. Let's start with atropine. A lot of us are familiar with the pharmacology involved, but I think for some of our listeners, they may either want to review or may they may not be familiar with it.

DR. MCALLISTER:

Sure. So atropine is a common drug that we see on our code cards every day and part of ACLS protocol for different scenarios. It's really the key drug of choice to treat the salivation and bronchospasm that is typically seen with patients exposed to these nerve agents. The very interesting thing that I've found was we typically think about treating patients with smaller doses of atropine. But it's important to remember that some of these patients that are exposed to sarin or may need extremely high doses of atropine in order to effectively treat them. And there are some military guidelines out there that suggest that sometimes as much as 100mg may be needed to effectively resolve the patient's symptoms. And the signs of inadequate response typically include seeing an elevation of the heart rate, typically above 90, and the presence of a dry mouth and skin. So you don't see the sweating and the salivating and that those are good signs that that you've reached a level of treatment.

DR. STRIKER:

Obviously, IV route would be most ideal. Are there other routes of atropine administration that one should consider in an instance like this? If IV access is unavailable?

DR. MCALLISTER:

I think there are potential for other routes of administration. Sure. As you mentioned, intravenous is preferred. Intraosseous is possible in cases where IV access is not able to be obtained. Endotracheal administration has been utilized in the past.

DR. STRIKER:

Many of us remember a movie called The Rock with Sean Connery, Nicolas Cage, Ed Harris. The premise was involving VX gas. And it's a movie. It's Hollywood. But the thing that was hammered home was injecting atropine into the heart directly. This is a little bit more of a tangent, but in your research, has that come up at all? Is that overblown? Is that necessary? Is there any... was there anything to that?

DR. MCALLISTER:

I think that's a little more Hollywood just for the extra sensationalism. I think Pulp Fiction may have used an intracardiac injection as part of their plot as well. Yeah, I think that's a that would be far down the list of places that I would prefer to do that.

DR. STRIKER:

On the subject of atropine, let's talk about other anticholinergics like Glycopyrrolate. Et cetera. Talk a little bit about those as options. Sure.

DR. MCALLISTER:

So, as you can imagine, if you're using super high doses of atropine to treat one patient, your pharmacy can quickly get depleted of the stockpile of atropine that they keep on hand. So I think it's important that we recall other anticholinergic agents that we may have at our disposal, and one that we use all the time is glycopyrrolate. The downside to that is it doesn't cross the blood brain barrier. Scopolamine, or even ipratropium are also anticholinergic agents that could be considered if your entire atropine stockpile has become depleted, especially in cases where it's a mass casualty and multiple victims exist. And then we often forget that other agents such as diphenhydramine or promethazine, also have anticholinergic properties. So while not the first line of defense or the first thing to consider, in extreme emergency that could be considered as part of the treatment regimen.

DR. STRIKER:

I also read something about lipid emulsion. Is that a realistic option?

DR. MCALLISTER:

Yeah. So organophosphate drugs are extremely lipid soluble. I've heard about this 15, 20 years ago. I'm a big proponent of lipid emulsion as treatment for local anesthetic systemic toxicity. And I've done a lot of reading and even some work with Dr. Guy Weinberg who came up with that treatment. And so there's been a lot of additional uses of lipid emulsion over the years that are very interesting. I recall reading about organophosphates being lipid soluble, and I did a literature search on it and actually found that there's some fairly good animal research being done out there about the effect of lipid emulsion on organophosphate poisoning. And there's actually one, at least one human case report of positive effects when lipid emulsion is combined with this, the standard treatment regimen. And the thinking is that in a type of situation where your atropine stock is being depleted, that lipid emulsion may allow you to use less of your atropine to get an effective treatment of the patient, thereby slowing down the depletion of your atropine stock. Obviously this is still in theoretical stages and is not out there in the literature being advocated for, but I thought it was very interesting to consider in a mass casualty type of situation.

DR. STRIKER:

Okay. Tupam, let's talk a little bit about that. What is it specifically, how does it work and what is the necessity of it?

DR. MCALLISTER:

Sure. So most people know Pralidoxime by the name that you you've mentioned, which is tupam, and it's an Oxime agent and also a vitally important part of the treatment regimen for nerve gas poisoning of organophosphates. The reason that Pralidoxime or tupam is so important is that it has the ability to reactivate the acetylcholinesterase enzyme. And as I mentioned, as a chemistry major, I also found this part very fascinating. And the way it does it chemically is it provides an oxime group in close proximity to that phosphorylated ester group that's on the enzyme, and in that way it can lure that phosphorus from its contact with that enzyme and that results in reactivation of that acetylcholine esterase enzyme.

DR. STRIKER:

Okay. Well, how necessary is that treatment and how should it be used?

DR. MCALLISTER:

So it's considered standard for nerve gas treatment. In my reading, I saw that patients can often recover without it, but if it's available, I think it's considered standard.

DR. STRIKER:

There's a time limit, right? You have to give it in a certain amount of time. Isn't that correct?

DR. MCALLISTER:

Right. Right. So there's a process that can occur. It's called aging, which results in making that reaction unable to occur and rendering Pralidoxime therapy ineffective. So it is very time sensitive. The exact timing is not completely known. But the idea is, as soon as you treat with atropine and get symptoms under control, you should be treating with pralidoxime as quickly as possible so that the aging hopefully will not occur. Once that conformational change has occurred, then it cannot go back and that phosphorus is kind of further encapsulated into that acetylcholinesterase and can't be as they as chemists say, can't be lured away from from that by that oxime group.

DR. STRIKER:

How available is Pralidoxime in ERs around the country and your typical institution?

DR. MCALLISTER:

I think it depends on each facility's policies, but I suspect that most hospitals have pralidoxime in their pharmacy. Now, as far as being prepared for a mass casualty attack, I'm not sure that pharmacies would be typically well equipped to deal with that. And likely if in that scenario, if there's multiple victims, there may have to be some transfers from other hospitals pharmacy stock in order to have enough on hand to treat the patients. Hopefully a large hospital would have pralidoxime and in ample amounts to effectively treat patients.

DR. STRIKER:

Okay. Well, we've talked about the pharmacology in the antidotes, if you will, for sarin exposure. What about basic management, airway management, etcetera?

DR. MCALLISTER:

We discussed about the anticipation that airway management is going to be needed and they'll probably have to be intubated and ventilated for a prolonged period of time. So I think most of us could examine this patient and and see that there's going to be

some challenges. And those challenges that occur with airway management are typically related to the symptoms of the poisoning and include the bronchospasm and the excessive salivation. We should likely expect some hemodynamic instability, most notably bradycardia. But if a patient's profoundly hypoxic, then complete cardiovascular collapse could be expected.

DR. STRIKER:

If you use muscle relaxant, what should we be using? Given the chemical effects of the organophosphate when it comes to the neuromuscular junction.

DR. MCALLISTER:

Normally with someone unable to protect their airway with excessive salivation, most people without if they don't understand the physiology of sarin or VX, they would reach for succinylcholine for a rapid sequence induction. However, with the pharmacology of succinylcholine, it's actually not advised to use it because it would likely worsen the problem by causing excess acetylcholine to be present at the neuromuscular junction. It may be that the poison's effects on the neuromuscular junction may actually lead to the desired effect and lead to some weakness or paralysis, giving you better intubating conditions without any pharmacologic intervention at all related to neuromuscular blockade.

DR. STRIKER:

Given the recent experience with anesthesiologists and Covid, we have become more adept at managing airways or just patient care in general with protective gear on. Maybe just talk a little bit about how that would look in something like this.

DR. MCALLISTER:

As you mentioned, during Covid, we dealt with airway management with all of this extra protective gear used by the healthcare team. As you would imagine, it results in less mobility and manual dexterity when you're wearing big suits, bulky protective suits and goggles and respirators. So I think our Covid experience likely gave us some semblance of what that might look like if we were to deal with sarin gas exposure. I think that it could act as kind of a trial run of how we would deal with that, because I think everybody now knows what it's like to be fully gowned and have decreased visibility through all of the protective gear that we have to deal with. So I think as a specialty, anesthesiologists are likely pretty prepared for that now.

DR. STRIKER:

Are there differences with the protective gear than what we're used to when it comes to a chemical exposure as opposed to a pathogen?

DR. MCALLISTER:

Yeah. So the chemical exposure, most notably, the one thing that I found in my reading was that our typical latex gloves that we use are ineffective at blocking the agents from penetrating through. So the recommendation is that you use these butyl rubber gloves, which are much, much thicker and much more resistant to penetration by the chemicals. But you also want to make sure you use protective eyewear, perhaps goggles, so that it's not about necessarily about splashing, but volatile gases that could get into your system through your eyes. And then you want to use a respirator mask or impervious gowns so that you're not getting any kind of skin or inhalation exposure.

DR. STRIKER:

We haven't talked much about the mass casualty preparation aspect of this. What would you suggest for organizations to do to prepare for something like this?

DR. MCALLISTER:

So I think most bigger hospitals have mass casualty drills and those are important and kind of expose weaknesses in your system so that you can identify those during your drills and so that if you do happen to have a mass casualty event, hopefully all of those weaknesses will have been identified and corrected. During these mass casualty drills, it's probably a good idea to consider incorporating the consideration of these nerve agents as part of the drill. And so doing that facility can identify some of the weaknesses in their team's response and also instill at least a baseline walking around knowledge of the processes that are important when considering the victims of these types of nerve gas attacks.

DR. STRIKER:

Well, before I let you go, I want to ask one last question, and that is how you chose to highlight this particular topic in ACE. In general, maybe comment a little bit about how you generally choose topics in ACE, but but why this one specifically?

DR. MCALLISTER:

Sure. So I like history of medicine and also like current events. And as I was reading, I found some information about sarin and I felt like the physiology and the pharmacology of these nerve agents are right in the wheelhouse of anesthesiologists because it's involving the neuromuscular junction and agents that we use every day. So I think we're, as a specialty, we're uniquely qualified to understand that physiology because we deal with it on a daily basis. That's what got me interested in it because I saw familiarity of some of the those items. I know some people may think that, well, this is not anesthesiology, and I don't have any idea why we're learning about sarin. But I think it is important to consider a few of these outside of the box type of topics that are only tangentially related to our specialty. I think it reminds us to think like physicians and to be ready to tackle and be a consultant on some more complex issues than our normal run of the mill scenarios. For that reason, I like to occasionally sprinkle in some obscure topics into our booklet. But typically, when I choose a topic for ACE, I most commonly choose something that is something that we deal with every day. It's only rarely that I choose a topic that is a little bit out there, like the sarin gas topic. I think it's important because when if it did happen, you're not going to have a lot of time to do a lot of searching on the Internet. It's going to happen quickly. And exposure of the health care team can happen quickly as well. So I think having at least a baseline knowledge can help protect the team. But it can also help you more effectively treat the patient.

DR. STRIKER:

Yeah, well stated. It's a fascinating topic. I think it's important that it highlights the unique expertise that anesthesiologists have in patient care. And it's not just the daily routine of things we do. It's oftentimes being the physicians of choice that are turned to in crises. And we saw that during Covid because of our unique ventilator and airway expertise. And I think in something like this, as you stated, we're well positioned to to be key players in a crisis like the one we've been talking about, heaven forbid, if it if it ever were to occur.

DR. MCALLISTER:

Thank you. I agree. I think it's important.

DR. STRIKER:

Well, Dr. McAllister, thank you so much for joining us to talk about this fascinating topic, very interesting from a scientific perspective. Really appreciate you taking the time and sharing your knowledge with us. And also thank you for everything you're doing for the ACE program. I know that's a significant commitment.

DR. MCALLISTER:

Sure. It's my pleasure to be here, and I appreciate being asked to join you. And I think the ACE product is great. And there's a great team of editors that are working hard to try and make it the best product that we can. And it's something I have valued greatly in the five years that I've been on on the editorial board, and I look forward to a few more years.

DR. STRIKER:

Excellent. To learn more about ACE, go to asahq.org/ace. Thank you for joining us on this episode of Central Line. Just a reminder to follow and subscribe on your favorite podcast platform and tune in again next time. Take care.

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VOICE OVER:

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