



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 to Central Line. I'm Dr. Adam Striker, your host and editor. And today I'm joined by Dr. Anuj Aggarwal. Dr. Aggarwal is a member of the ACE editorial board and a pain specialist at Stanford University. He wrote two opioid focused items appearing in the latest issue of ACE. And I wanted to learn more about the topics. So I invited him to join me today. And for those of you who may not remember, ACE stands for Anesthesia Continuing Education. Dr. Aggarwal, welcome to the show.

DR. AGGARWAL:

Thanks, Dr. Striker Thanks for having me.

DR. STRIKER:

Yeah, certainly. Before we delve into the topic, do you mind telling us a little bit about your background and your experience with ACE?

DR. AGGARWAL:

Yeah, I'm a practicing chronic pain physician. I also practice general anesthesia in the OR at Stanford. As you mentioned, I specialize in orofacial pain, but I have a specialty and interest in pharmacology. I oversee and direct the curriculum for pharmacology education at the medical school at Stanford. And I've been a part of ACE now for about two years. And like to read the right questions about pharmacology, anesthesia, and sort of current changes and new topics that are developing within our field.

DR. STRIKER:

And you contributed a few items on the topic of opioids to the new issue of ACE. Opioids is obviously such a large topic and it's an important one. Why don't you start by telling us, in your words, why the issue of opioids is still so salient? What do you think that we should be focusing on?

DR. AGGARWAL:

Yeah, I think the reason opioids are such a salient topic is that in many ways they're the oldest of medications we've we use in medicine. We've used them for thousands of years. And part of it is because they're so powerful, they have so many effects, and they really go to some of our most core physiological functions. Motivation, behavior, how we interpret the world, our interpretation and experience of pain, and our response to stress. And so the use of opioids is really central to the practice of modern medicine. It allows us to do surgery and anesthesia, as all of us know. But the salience to me is really around that, I think there's a misunderstanding often that we know a lot about these medications because we've used them for so long. But actually our use of the medication predates our understanding of them. And as we understand more and more about the molecular and scientific underpinnings of how opioids work, I think we've come to realize that they're much more complicated pharmacological agents than we perceived. And it really comes to light when we think about something such as the opioid epidemic. This really transient problem in American and even in other societies of the role that opioids play when they interact with us at an individual community and then at a national level.

DR. STRIKER:

I do want to get to, you know, a few specific items. One of them is a new opioid that's on the market called Olceridine, trade name is Olynvic. From what I understand, it's the first in a new class of opioids approved by the FDA. Why don't you go ahead and tell us a little bit about this particular drug and how how it differs from our conventional opioids?

DR. AGGARWAL:

Yeah, Olceridine is the sort of new opioid that's on the market, and it is in a sort of inherited vein of us--and by us means to the scientific community--trying to develop a better opioid sort of the holy grail of developing an opioid that can give us all of the great effects that we desire of opioids, namely analgesia, without the adverse effects that we associate with opioids, including dependence, euphoria, respiratory depression and perhaps sedation.

And for a very long time, you know, once we you know, in the 70s we really discovered the opioid receptors, the various subtypes of the opioid receptors. And as we started to figure out that opioid receptors are g-protein coupled receptors, we started to detangle the molecular underpinnings of opioids from the drugs themselves. And I think many of us learned in medical school, sort of all of those secondary messenger systems and how g-protein coupled receptors work. But as the science evolved, particularly in the 90 seconds and the early 2000, we actually came to realize that these receptors are much more complicated and that while opioid receptors are g-protein coupled receptors and have pathways that go via the g-protein, they also have other different types of pathways, particularly a beta arrestin pathway. And some early work showed that perhaps the analgesia from opioids was mediated via this g-protein dependent pathway, but that some of the adverse effects, namely respiratory depression, were mediated via the beta arrestin pathway. And this began this sort of race to see could we develop an opioid that could preferentially activate the analgesic pathway without the respiratory depression pathway. And Oliceridine is in this vein of being what we call a biased agonist, meaning it biases itself towards one pathway versus the other in the hopes of developing, quote unquote, a safer opioid.

DR. STRIKER:

That's actually a label, from what I understand, biased ligand label.

DR. AGGARWAL:

The FDA has given it sort of a label. If you look at the packaging of it, that it is the mechanism of action is that it's a biased opioid agent, correct.

DR. STRIKER:

And it's not proven. This is still a theory. The g-protein versus the beta arrestin pathway that.

DR. AGGARWAL:

Yeah, well, like with everything I think, you know, as we discover more and more things can seem very clear at the beginning and as we gain experience with them, we start to realize that the story is more complicated. So very similarly, you know, the story was actually we discovered morphine and then we discovered heroin or diacetylmorphine and diacetylmorphine or heroin was marketed as a safer alternative to morphine, extended release Oxycodone was in the 90s and marketed as a safer, maybe alternative to oxycodone, immediate release. We sort of been down this road before.

And essentially what happened was really at the turn, going from the 90s to the early 2000, there was a lot of animal data showing a lot of promise around this biased agonism that if you could really preferentially get just the g-protein pathway, you would have a lot of safety margin. And the drug development really started to take off around that period of time. Now we're about 20 years ahead. And in that 20 years, what's happened is that this theory of biased agonism has become much more complicated in that we've discovered there's other pathways that it's not a very it's not a clean, biased agonism. And with all opioid medications, the story is a little bit more complicated. And while things may have a little bit more safety, it may only be around one adverse effect. But because opioids have so many different adverse effects to be able to globally say they're much safer, becomes a much more complicated label or question to answer.

DR. STRIKER:

Yeah like everything it's it's simple for us to all think about when it's linear or there's one variable, if you will, and then you start introducing the other variables, everything becomes more complicated. Obviously, this is no different. Let's talk about clinical use of Olinvyk. How is it administered IV, orally? How is it going to be utilized in the clinical realm?

DR. AGGARWAL:

Yeah. So it's an intravenous only medication and it's been approved essentially by the FDA for management of pain in acute settings, particularly around post-operative pain. The studies that were done with Oliceridine were really done around utilization in pca systems. So clinically, the way the FDA has approved it and sort of I perceive that it's going to be introduced into clinical use is really going to be around acute pain management in the PACU post-operative period as well as within a monitored hospital setting. Given that the comparative advantage theoretically of the medication is that it may have less respiratory depression. The issue was that the clinical trials weren't really well powered to study decreased incidence of both respiratory depression or constipation. And there are some mixed findings that we found. But when you actually look at their efficacy of Oliceridine to treat pain, it's pretty effective when you compare it to morphine, very similar whether or not it's safer and resulted in less side effects. It's actually sort of a mixed question, but it got the FDA label of the unique mechanism of action.

DR. STRIKER:

When I was reading about the FDA approval or the indications, it's indicated when other traditional pain medications have failed. Is that correct?

DR. AGGARWAL:

You know I think this is one of the complicated issues around the approval of new opioids or new medications for pain that they generally get this labeling that it's approved when other traditional medications have been proven to be ineffective. However, I think what we find in practical, real world clinical use is that these medications get quickly substituted or can be substituted as first line. But yes, the official labeling would be that if for individuals who have not had an adequate response or have had significant adverse effects to what we would consider our traditional medications.

DR. STRIKER:

Because of the particular intravenous use in an inpatient setting, it won't be that won't be necessarily a barrier to its use.

DR. AGGARWAL:

I don't think so. But I think to me, the central portion of it is thinking that it's much safer. And I think historically we've fallen into this trap before about thinking that a new opioid was safer. And I think clinically at times it has lowered our caution and our guardrails around the use of opioids. And given that there is research and data showing that the intensity of use of opioids and duration of use of opioids are factors in prolonged use of opioids after surgery, including other risk factors that are patient dependent, falling into the trap that, oh, we have a new safe opioid when the reality is we're actually still learning about its use and its effects in humans, particularly in large patient populations, I think just wants us to understand that this is a new tool. It works a little bit differently. But it's unclear how and why this is. You know, while the FDA has given it the labeling and in the package insert about the fact that it's a biased opioid agonist, there's actually some controversy around that within the sort of basic science committee. There are pharmacologists and researchers who say that Oliceridine effect might not actually be due to biased agonism, but it actually might just be because it's a partial agonist similar to buprenorphine. And we know that buprenorphine has significantly less respiratory depression and GI side effects compared to our traditional opioids as well. And it's just sort of goes to the fact that while a nice story would be very convenient and it sort of has this labeling of the nice story, perhaps the science isn't quite there and the science is a little bit more uncertain and skeptical about exactly how this medication may work.

DR. STRIKER:

Sounds interesting. Well, we'll certainly have to see how that all plays out. I do want to shift gears a little bit and talk about long term opioid use, especially after surgery. Let's do that right after a short patient safety break. So please stay with me.

(SOUNDBITE OF MUSIC)

DR. JEFF GREEN:

Hi, this is Dr. Jeff Green with the ASA Patient Safety Editorial Board. We can learn from errors, near misses and adverse events by using formal analysis of the unreliable systems that played a role in the scenario. Through error analysis we can investigate errors, identify and address their causes, and prevent future occurrences of similar events. Root cause analysis is a detailed retrospective review of an event by a multidisciplinary team using tools such as the Five Whys and the Ishikawa or Fishbone diagram to identify and repair the underlying or root causes of errors. Failure mode effect analysis is a prospective process using subject matter experts to identify weakness in a process where system failure could occur by measuring the frequency, severity and detectability of failure points. The discipline of human factors engineering can assist in the development of safety systems that prevent inevitable human errors from reaching the patient and causing harm. It's a worthy endeavor for health care to adopt the goal of achieving zero events of preventable harm.

VOICE OVER:

For more information on patient safety, visit [asahq.org/patientsafet22](http://asahq.org/patientsafet22).

DR. STRIKER:

Okay. We're back talking with Dr. Aggarwal on the topic of opioids. I wanted to talk a little bit about long term opioid use after surgery. What do you think the listeners, mainly anesthesiologists of this podcast, should be on the lookout for when it comes to this topic?

DR. AGGARWAL:

Yeah. You know, I think there's been a lot of appropriate focus on the use of opioids in the perioperative period. Particularly as we've rightfully embraced our role as perioperative physicians, our ability to modify and change the trajectory of individuals after surgery becomes more and more important. And I think opioids is a place where anesthesiologists have done a lot of excellent work in regards to reducing the exposure

of individuals to opioids and helping guide our surgical colleagues into safer prescribing practices upon discharge. And I think while there's been a lot of focus around reducing the intensity of pain after surgery and reducing the exposure of opioids to individuals after surgery, there's increasing data to suggest that there are other factors, namely that there are vulnerable, potentially vulnerable patient populations who may be more likely to continue to use opioids for a prolonged period of time after surgery, putting them at risk of developing an opioid dependence or a new opioid addiction. And again, it's one of those places where, as we study it, more things come into more focus and we figure things out with a little bit more detail. But clearly there seem to be certain risk factors that patients bring to surgery that put them at risk of utilizing opioids for prolonged periods of time after surgery. And I think as anesthesiologists, we can help identify these patients when we evaluate them before surgery and perhaps develop programs to better guide these patients throughout the perioperative period.

DR. STRIKER:

You know, it's interesting because what you're describing is our shift in focus from perhaps case based anesthesia to patient based anesthesia, which is something we as anesthesiologists should always be doing. But we tend to fall into the trap of basing our treatment or the anesthetic to a great degree on the case we're doing. This is what I usually do for this surgery. This is what I usually give my patients when they have this done. It certainly sounds like this is one of those aspects of anesthetic care that could really hammer home that shift in thinking as we know more about it and the practice changes that it probably I imagine it will shift our focus as practicing anesthesiologists even more towards the patient per se. Do you think that's right?

DR. AGGARWAL:

I think so. I mean, I think I would say that we actually in some ways, we do this already. You know, in some ways, when we think about a patient who is coming in for surgery and may have multiple, we would say sort of cardiac risk factors, we change our anesthetic and we have developed systems to help ensure that those patients go through surgery safely. And I think when it comes to pain, I think for very understandable reasons, we've focused really on pain. Once the individual starts feeling pain or starts reporting pain. And I think there's this over the past really decade, there's been this shift towards thinking, why can't we plan for patients pain before they have the pain? And taking it one step further, thinking about, well, what are risk factors for patients to have complicated pain management cases and histories after surgery? And so to me, in many ways, when I do an anesthetic or I'm planning an anesthetic, it's the same way I would think about, well, this patient has multiple cardiac risk factors. I sort of think about, well, does this patient have risk factors for prolonged opioid use or

increased pain, perhaps things such as preoperative use of benzodiazepines, preoperative use of antidepressants, history of depression, history of substance use disorder, and seeing if we can partner with our surgical colleagues and within our systems to develop appropriate pathways that can ensure that these patients get the best care. Understanding that our responsibility is not just in the operating room, but it really goes on to see how these patients do long term after their surgeries as well.

DR. STRIKER:

Do you think that that's well understood throughout the anesthesia community when it comes to pain specifically, maybe as opposed to other aspects of the anesthetic? Or is this something that you think we still need to work on as a community of practicing physicians?

DR. AGGARWAL:

I think we've made significant strides. We've introduced opioid sparing techniques, the explosion and use of regional anesthetic techniques, the focus on opioid cessation and tapering after surgery. But I think the piece that we as a specialty have a lot more work to do is in that preoperative period. And I think for a long time it was because all we could do was really identify the risk factors. But question was, could you intervene and do something before surgery? And this is where I think the data is starting to emerge that, yes, actually we can have interventions before surgery that can improve outcomes after surgery. And you know, the question, what I wrote for ACE was really about identifying the preoperative risk factors. It's because I think what we're going to see over the next ten years is the research really starting to come out showing that guided specific interventions, things such as psychological interventions, interventions with our addiction colleagues in at risk individuals, self-guided educational interventions for patients who are at risk of prolonged opioid use after surgery are going to result in better outcomes for these patients. And so while we've focused a lot on cessation of opioids after surgery and we've focused a lot on identifying some of those risk factors, I think where our specialty is starting to see data emerge and where the movement is going to be is about intervening before surgery to help improve outcomes after surgery.

DR. STRIKER:

Now, do you think certain patients are getting opioids discontinued too soon after surgery because of this concern? In other words, there are certain patients who may not be as much at risk for issues afterward when it comes to, you know, opioid usage. So are we being too constrained when it comes to some of our post-operative patients and the need for certain pain medications?



DR. AGGARWAL:

I think this is sort of a huge question about opioid prescribing. It really appeared for a long time that almost all of us in the post-operative period were too generous. We were over prescribing opioids and patients weren't using the amount of opioids that we were prescribing. And over really the past decade, there's been a steep decline overall in American medicine about around the prescription of opioids in many places, very rightfully so. And a lot of that has been by giving guidance to prescribers who mainly are not actually us as anesthesiologists, but our surgical colleagues around how much and how often should patients be taking opioids after certain types of surgeries? Sort of to go to your point, Dr. Striker, that case based surgical anesthetic and perioperative or post-operative care. I think what we are starting to see, though, is perhaps an overapplication of pathways and protocols to all patients. You have a certain type of surgery, say a knee replacement, you get X amount of opioids and that's it that everybody's going to fall into that pathway. But we all sort of know that there are patients who are not going to fall into that pathway. And there's one thing about identifying them once they're already using more opioid or are not tapering off their opioid as expected. But I think there's sort of a shift into thinking, well, how many of these people could we have predicted would not have fallen into these pathways or the expected protocols, and thus should we have different protocols or different interventions for these individuals so that they get the more appropriate level of care and perhaps more intensive care than the majority of patients may need, particularly around pain management or opioid prescribing.

DR. STRIKER:

Right. And certainly opens up another few avenues of discussion, potentially the protocols and and how we're applying them to different patients. But I see a lot of chatter, whether it's social media or discussion boards or at meetings about, you know, the use of opioids. It seems like some really believe in minimizing opioid use and some are advocates of liberal opioid use when needed. I would imagine, you know, the right approach is like we talked about patient based and it's probably part of a comprehensive plan. I guess I just want to get your take on this idea of minimizing opioids. Is that the right term we should be using or is it should it be just appropriate use of opioids? It's kind of more of a philosophical question in how we how we address the topic, I guess.

DR. AGGARWAL:

No, I think, Dr. Striker, it's such a great question. And I think if you asked ten physicians, you would get ten different philosophies around opioids. One of the guiding cornerstones to me around opioids is, first, understanding that opioids are not pain medications. I think when we think about opioids as pain medications, we fall into the trap of, well, you just give it and the patient's pain gets better. And that's not what opioids are. Opioids are simply medications that work on the opioid receptor, and they have a myriad of effects. We use Loperamide to treat diarrhea, which is an opioid. And so opioids are not just for pain. And so the first thing to me about philosophically is they're not pain medications, they're opioids, and they work on the opioid receptor. And so then what do opioid receptors in our body do? They really modulate in many ways our response to stress. And one of those elements is modulating our experience of pain. And so for me, I think about the appropriate use of opioids is to help modulate and change the experience of pain for our patients after surgery. And then the question is to what end and to what goal? And to me, the goal of surgery is recovery and appropriate healing. It is not to eliminate pain. And so. When think about opioid prescribing after surgery, to me the goal is opioids should be prescribed appropriately and at the right amount so that the experience of a patient's pain is modulated to the appropriate degree so that they're able to achieve our post-surgical goals. And to me, post-surgical goals are not the elimination of pain or to be pain free. Pain is a part of our healing process. It does not mean that patients need to suffer, but it also doesn't need to mean that they can't experience any pain. And part of that's preparing patients for surgery as well. To understand that patients need to go into surgery expecting a degree of pain as part of their healing process. And so to me, it's not about being restrictive or being about liberal, about opioids. Similarly, as we aren't restrictive or liberal about other medications. It's about using them appropriately to get the goal that we have in mind and perhaps changing it to reducing or eliminating pain, to changing our goal to helping patients achieve the goal of the surgery is a way to help guide our prescribing of opioids.

DR. STRIKER:

Well, do you think that we do a good job as anesthesiologists in preparing the patients for that or creating realistic expectations in that regard? There's obviously a lot of yield to doing that, but do you think that we have a long way to go or are we doing a pretty good job of that?

DR. AGGARWAL:

I think this is a place that not just us as anesthesiologists, but I think us as a larger medical community have work to do. You know, I remember when I was training as a resident, which was not very long ago, and even when I was in medical school, there

was, you know, a lot of talk about like painless surgery, pain free surgery. You're going to be completely comfortable after surgery. You've got all these new techniques and technologies with and the explosion of regional anesthetics, etcetera, that you won't be you won't have any discomfort after surgery. And and I think that sort of does a disservice to our patients in many ways where pain is a normal part of that healing and sort of I think we as medicine can do a better job of preparing our patients to have realistic expectations after surgery. I think it's it's something that makes me very uncomfortable to talk to patients that, you know, it's not going to be everything's not going to be perfect after surgery. You're going to have some discomfort. It's going to be a recovery. But I think what we've seen and there's some research coming out that the more you prepare patients before surgery and the more that they have realistic expectations around recovery after surgery, they actually have less pain and they do better after surgery. I think as a global medical community, I think we have some work to do around setting realistic expectations after surgery. But we've made definitely strides, particularly over the last 10 to 15 years, around understanding that patients need to be prepared for what is going to be after surgery.

DR. STRIKER:

Do you think our surgical colleagues share that sentiment in general? That's obviously an area that we should certainly target. But is that something that needs a lot of work, or do you think they're doing a good job of preparing patients for the surgeries they're having?

DR. AGGARWAL:

I think as anesthesiologists, we have a lot to offer our surgical colleagues. Our surgical colleagues are amazing at what they do, but sometimes they aren't thinking as completely about the perioperative experience. And I think as a specialty that that's really where we come in. And where I think sometimes see the disconnect is there are not robust systems in place for a variety of reasons that go beyond just our training and what we think should be done, but also around reimbursement and funding and logistics and staffing. But I don't believe there are enough robust systems to catch and identify patients preoperatively around pain and then to have timely and robust tools to have patients be consulted on and intervened on after surgery who seem to be at risk and not following the appropriate pathways that most of our surgical patients would seem to follow. I mean, I think these are just in general, really challenging systems-based problems. But that's where I think anesthesiologists have really succeeded, is in many ways in building robust systems that have increased patient safety and looking at pain as a component of patient safety. And, you know, when I look at the national landscape, I see a lot of exciting work by a lot of our colleagues who are looking at this space. I see

some positive movement, but I think we're in the early stages of what these systems are going to end up looking like in ten, 20 years.

DR. STRIKER:

As you stated, we offer such a breadth of expertise when it comes to the perioperative arena. And the reason I ask about the surgical colleagues is obviously just because they're the ones that see the patients first, they're the ones that bring the patients to us and we see them in a short period of time before the actual operation, typically in the acute setting. Yet, it sounds like there are plenty of opportunity for for us as perioperative experts to to weigh in in some fashion, whatever the system is, a little bit ahead of time to try to optimize the patient experience.

DR. AGGARWAL:

Yeah. And I think we've sort of led and assisted our surgical colleagues in understanding the types of patients who may need more evaluation for elective surgery around cardiac risk factors, pulmonary risk factors, etcetera. I think we on an individual basis can, within the places and systems that we practice, help educate our surgical colleagues, perhaps around some of the risk factors that may result in more pain or really prolonged opioid use after surgery to alert the surgeons, just as you identified Dr. Striker, because they were the ones who are first interacting with these patients in the perioperative period to think about like, well, maybe this patient seems to have certain risk factors, perhaps we should consult somebody, consult somebody in our anesthesia group who can maybe connect with a pain specialist or an acute pain specialist and see, is there something that we can do prior to surgery to get them ready for what is to come? And I think some of those little things that we all do actually on a day to day basis, as we make those relationships with our surgical colleagues, with the types of cases that we do in our various practices, I think this is where something that appears as simple as being like, well, what are the risk factors or what do we understand to be the risk factors of prolonged opioid use can become really quite important in those conversations as we make those relationships and have those relationships with our surgical colleagues.

DR. STRIKER:

Yeah. And just another further example of how the science of anesthesiology, no matter how much we try to simplify it, or how much it appears to be simple, it continues to take on complexities and continues to be a work necessitating further investigation and study and a constant evolution of care giving. And why, you know, I still think it's one of those arenas that does not seem like there's much more to learn and yet always fascinated

that when you look, there does appear to always be more to learn and more to figure out and still tons of mystery.

DR. AGGARWAL:

Yeah. And I think, you know, being on the ACE editorial board, that's been one of the joys is to continue to explore as the science of our specialty evolves and as new issues face our society. And and we as anesthesiologists respond to those issues facing our society. Everything from, you know, I think a lot about the opioid epidemic. But as our specialty responded to the COVID pandemic, for me, when I write or write my ACE questions, I'm often thinking about, well, where is the science today? What are the scientific principles that we've known for a long time and how are they still relevant and evolving to our practice as new issues, new technologies, new drugs come to our specialty and affect how we're going to be able to deliver better, safer, more equitable care.

DR. STRIKER:

Yeah, absolutely. Well, along those lines. Before I let you go, let's talk just a tiny bit more about the ACE process. And you already alluded to just now how you choose maybe the topics you write on, but are there some specific thoughts with, when you finalize a question or why you choose a specific kind of a question versus another? What what other little nuggets can you offer us as to what goes into your thought process when you finalize questions?

DR. AGGARWAL:

Dr. Striker When I'm thinking about the ACE questions, I'm trying to balance relevance to most of, you know, our community as practicing anesthesiologists and also balancing sort of that edge of where is the science today and what's changing. And one of the things that may be a little bit sort of mysterious is like some of these questions may seem like like the question about that, onne question that I wrote about Oliceridine, is like, well, you know, I don't have it in my practice or this is going to be this might be an expensive drug. We're not going to see it. But to me, when I'm thinking about the questions, it's not necessarily about that the specific procedure or the specific drug itself, but it's really about like, what's the basic concept and how is that basic concept changing around how do opioids work and what may be in the talk, or when individuals are going to meetings, or they're getting marketing materials from companies, what are they going to be seeing? And so when I'm picking and thinking about an ACE question, it's about trying to help my colleagues keep up to date and process the large amount of science and material that's coming into our specialty while making sure that we continue

to refresh for myself and also for my colleagues around the core concepts that we use every single day in practice. And, you know, when we have our meetings and all of the editors talk, part of what we come to realize is our field is continuing to change every single month and every single year. And all of us need to keep abreast of the latest developments and the latest scientific advances. But at the same time, we can't forget the very basics and the very foundations of our specialty. And so we try to balance the two when we write our questions for our colleagues as part of the ACE questions.

DR. STRIKER:

Well, Dr. Aggarwal, it's been a fascinating discussion. And so I just want to thank you for all your time.

DR. AGGARWAL:

Thank you so much, Dr. Striker, for having me. It was my pleasure.

(SOUNDBITE OF MUSIC)

DR. STRIKER:

And this issue. Ace, 28, publishes in early April, just like this podcast. And for listeners interested in learning more, visit [asahq.org/ace](http://asahq.org/ace) or A.C.E. for more information on this topic and many other topics that this issue touches on.

To all our listeners, thanks for tuning in to this episode of Central Line. Please tune in again next time and take care.

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