#366 Opioid Use Disorder and Acute Pain in the Hospitalized Patient

[The Curbsiders Podcast theme]

Matthew: Welcome back to The Curbsiders. On tonight's show, I will be talking to two fantastic guests about how we can treat acute pain in the patient with opioid use disorder who's admitted to the hospital.

I, of course, am Dr. Matthew Frank Watto. Unfortunately, tonight without my fantastic cohost, Dr. Paul Nelson Williams. So, I will remind you that we are The Internal Medicine Podcast. We use expert interviews to bring you clinical pearls and practice-changing knowledge.

On tonight's show, I have a great conversation with Dr. Carolyn Chan and Dr. Shawn Cohen, who are going to tell us all about how to handle this very common and very challenging problem in the hospital, patients who are both either in opioid withdrawal or at risk for opioid withdrawal and also having an acute painful condition. So, they're going to tell us how to treat both those things. It's a really fantastic conversation. Not going to get into the full bios, because Shawn and Carolyn are going to tell you about themselves. A reminder that this and most episodes will be available for free CME credit for all health professionals through VCU Health at *curbsiders.vcuhealth.org*.

Carolyn, Shawn, we've been talking for a while here, but let's get the audience in on this and please tell them-- Carolyn, let's start with you. Give the audience like a one-liner. Let them know what you do for your job and tell them maybe a hobby or interest as well.

Carolyn: I am a 33-year-old internist and addiction medicine doctor. I currently am a medical education fellow and I love eating ice cream and strongly believe that you should be able to eat it in all seasons. [Matthew laughs] In my other free time, I like to do improv comedy and I cohost the Curbsiders Addiction Medicine series with one of my colleagues here today.

Matthew: Which is not an improv comedy series.

[laughter]

Carolyn: Yeah, that is correct.

Matthew: Right. Yes. We're excited to have both of you on. It's been a great Addiction Medicine series. Hopefully, more to come from that. This is a teaser for the audience in between seasons. I think this will be very helpful to a lot of people listening. So, also with us is Dr. Shawn Cohen. Shawn, can you give the audience a one-liner and maybe a hobby or interest?

Shawn: Yeah. I always have to recalculate my age every time I do it nowadays, which I assume means once you get your 30s, maybe you start doing that. But I think I'm also a 33-year-old. I am an aspiring dad joker and much like Carolyn, a formally burned-out hospitalist you really re-found my love for medicine in helping people with substance use disorders in the hospital and going back to addiction med fellowship. I also go to Carolyn for all of my ice cream advice. [Matthew laughs] I ride her coattails like doing this podcast with her. So, my big hobby now is probably, most of my time is just spent taking care of my, not so terrible two-year-old.

Matthew: All right. And part of the genesis for this podcast as I was telling you guys before was as I spend some of my time as a hospitalist, I talk to other hospitals. I know that it's a tough thing. You have patients admitted to the hospital, they're in acute pain, but they also have substance like opioid use

disorder and you're trying to manage both those things at the same time. So, we're going to go through some cases that give us a couple common scenarios.

Since Paul's not here, I will read the first case here. This first case, JJ, a 32-year-old male. He has severe opioid use disorder. He's already on buprenorphine and naloxone 8 milligrams twice a day, smokes a pack a day of cigarettes, occasional alcohol. He's had endocarditis in the past and has been admitted with sepsis from a thoracic epidural abscess. He has spine tenderness, saying his pain is like 7 out of 10. Of course, we start him on aggressive nicotine replacement, which I find is always essential. But we think he's going to need surgery, so we need acute pain control.

Now, the old teaching and I know we've covered this a little bit on the show, but maybe people haven't heard those old ones. The old teaching was stop buprenorphine because you're not going to be able to give full agonist opioids like morphine, like hydromorphone. Carolyn, what's the current thinking on this now?

Carolyn: Currently, we think that we should continue it throughout the perioperative, postoperative period for our patients, because we know from more clinical experience now that we can indeed achieve adequate analgesia by maintaining folks on their MOUD and also treating their acute pain with full agonist on top.

Matthew: Yeah, and I gave an example, so full agonist, the hydromorphone, morphine, fentanyl, of course-- Now, fentanyl, we're not thinking of it as a pharmaceutical, but it is. Shawn, can you remind people of the pharmacology like why do they think buprenorphine isn't going to allow people to get full agonist effects or adequate pain control if they have buprenorphine in their system?

Shawn: Yeah. Buprenorphine is a partial agonist at the opioid receptor, but it's also super high affinity. And so, I described it as clamps onto that opioid receptor and binds tighter. There's a thought that if all of your opioid receptors are filled with buprenorphine, no other opioids can get on and you can't get pain control, but the reality is, nothing is static. The opioid receptors are changing all the time and what's on them is changing and so you can still give full agonist and get pain control too.

I think the other thing to really keep in mind is that if you're stopping someone's buprenorphine, like getting people back onto buprenorphine is another step in the process. And now that we know that the recommendation is to keep people on Bupe throughout, there have been these bigger studies that show that that's not the case for I think greater than 60% of people that Bupe is stopped and a big chunk of them don't get back onto Bupe. I think there was this study out of The Journal of General Internal Medicine where over 10% never got back onto Bupe and then 5% died from overdose within the follow-up period.

This is a critical thing that we need to change our practice on. People should stay on buprenorphine. You can use full agonists, higher affinity stuff, like hydromorphone and fentanyl for pain, and all the other stuff that we always use for pain too. Tylenol, NSAIDs, try to get anesthesia involved for nerve blocks.

Matthew: So, JJ is on 8 milligrams twice a day and we want to keep him on the buprenorphine. Carolyn, do you like to split it up? I know buprenorphine provides six to eight hours of analgesic effect. Do you split it up? And if so, what's something typical you do for a patient like JJ?

Carolyn: Yeah, that's a great question. The first thing I do is I ask the patient and I talk to them about this. If a patient feels strongly that they don't want to change their medication or home dose at all, I don't feel strongly that we have to split it. I often like to try it and I recommend it as an option to patients to say, "Hey, we may get improved control of your pain by splitting." So, generally, my approach is to start with their original home dose. Okay. So, let's say, he's on 16 milligrams total daily dose, could split this a couple of ways. I would offer him possibly doing 4 milligrams every six hours or 8 milligrams, 4 milligrams and 4 milligrams for TID dosing as a starting point.

Matthew: I've seen some people go up above that. To me that I was afraid to do that, because if I go up on their dose, then what does that mean for their outpatient? Are they going to have to be discharged on that? That's where my head would be going if I'm thinking about this. I'd love to hear how you approach that.

Carolyn: I like to think of it in terms of two buckets. One, I want to make sure I'm treating their opioid use disorder and then the other bucket, two, is treating their pain. If somebody's opioid use disorder was not well controlled, they were still having cravings, having intermittent use. I'm going to automatically offer to increase that dose of buprenorphine for them, because I already was probably not treating their opioid use disorder adequately. And then generally, I think about treating the pain, the acute pain again in the second bucket.

I like to think a lot about that pain generator. I do think that has a role. If somebody is having CT surgery for endocarditis, that's a very different type of pain than if somebody has cellulitis and we think it's going to really improve over the next couple of days with adequate antibiotic treatment. So, if it's more on the mild side in my expert opinion, I will offer a higher dose for acute pain. I will also offer a higher dose to treat undertreated opioid use disorder. If the patient I think is going to have a more moderate to severe pain generator, then I am really thinking maybe I'll start by just keeping the buprenorphine the same and then adding the full agonist on top.

Matthew: Shawn, what about you? Anything different about your approach to that?

Shawn: Yeah, I think I trained in the same place that Carolyn did. So, I think our approaches are often similar. I don't know that I had a formalized framework, but that is what I do. I think I don't worry about changing people's buprenorphine dose and increasing that, but I think I'm also fortunate in that I work at a place where there's very easy access to buprenorphine and pretty seamless communication with a lot of the buprenorphine prescribers in the area where I can just say, "I increase their dose to 24 and someone will take over." I know that's not the case everywhere.

I think if someone was nervous about someone leaving on a higher dose of buprenorphine, you can always call their prescriber too, although that's an extra step in another very busy hospitalist day I'm sure. But I think I'll do the same thing as Carolyn is. If the pain is mild or moderate, try increasing the

dose. If that doesn't work, maybe add an opioid. If I think the pain is going to be as severe, just add an opioid right away. And again, in addition to adding all the other things for pain that we should be doing too.

Matthew: Let's say for instance, we put JJ on 4 milligrams four times a day, we haven't changed the home dose and for whatever reason, we decide instead of going up to 24 milligrams or 8 milligrams three times a day of the buprenorphine, we decide we want to give something short acting for pain on top of it. Is there any preference like IV, oral? Should all that work just the same? Can we give oxycodone just as well as we can give IV hydrocodone or hydromorphone rather? Shawn, what do you think?

Shawn: Yeah. I don't know if there's firm data supporting this, but the thought is that higher affinity. So, Bupe has really high affinity at the opioid receptor. If you want to use an opioid that competes with it at the opioid receptor to get good pain control, the thought is, the two opioids that we can prescribe that have the highest affinity are hydromorphone, which you can generally use in any clinical area in the hospital and then fentanyl, usually IV, which at least the hospitals I worked at is usually limited to the ED and ICU or the step-down unit. And so, I usually reach for hydromorphone predominantly.

I don't think there's a big difference, at least in my knowledge between using oral and using IV. I always opt for oral when people can take oral more because it just last longer. If you're using IV, you have to dose every two hours and people just go on these rollercoaster rides of having their pain controlled and then not controlled and then pain-- So, I think as long as you dose it in the appropriate intervals, it works better in general.

Matthew: Yeah. So, those intervals every two to four hours something like that. Hopefully, with the orals, they get every three to four hours, at least three to four hours of pain control.

Shawn: Yeah.

Matthew: Yes.

Carolyn: I will say, it's okay to do both. We have had patients right with complex wound dressings, who need a dose of IV medications to really help them in those situations. So, I will definitely still use a combination. Reach for oral first, but I will still use IV as needed if there's severe breakthrough pain.

Matthew: Okay.

Shawn: I think I use IV too when I'm first meeting a patient, they're first coming out the OR and I get them on an oral regimen, but I don't know what dose is going to work for them. And so, I'll start them on some orals, but have the IV as back up too, so I can start ramping up to get the oral dose that they eventually need.

Matthew: Okay. Great. We're addressing their opioid cravings with the buprenorphine. That also is doing a little work for the pain if we give it in the split dosing and then we're using a full agonist opioid

on top of that something that's hydromorphone, fentanyl have maybe a little more higher affinity. And then the other question is like PCA, I've heard that that might be something that some people are using as well for-- If he's going for a thoracic surgery, maybe this is going to be a really painful wound to recover from. Should that be on the table as well? For someone with opioid use disorder, giving them IV opioids always feels a little scary. Are we going to stimulate more craving? So, what do y'all think about that, the PCA?

Carolyn: I think you should use the PCA for a patient, an individual who has opioid use disorder and the exact same situation in which you would use a PCA for an individual who doesn't have an opioid use disorder.

Matthew: Okay.

Carolyn: The person already has an opioid use disorder, if anything, I think we're putting them at risk by not adequately controlling their pain.

Matthew: Okay.

Carolyn: If we aren't controlling their pain, we're putting them at risk of prematurely leaving the hospital, supplementing in the hospital with other substances.

Shawn: I think the hospital I used to work out when I was a hospitalist, PCAs could only be ordered really by the pain service. And so, I think it'll depend on what's available at your hospital to knowing that with any opioid, when someone has an opioid tolerance is on MOUD, they're going to need higher doses. And so, they'll probably need higher doses of the PCA too. So, you probably have to work in a multidisciplinary team to sort that out a little bit more.

Matthew: Well, JJ, we're going to switch his case up in a little bit here. If we did put JJ on 8 milligrams of Bupe, which was an increase in his dose 8 three times a day instead of 8 twice a day, which he was taking at home. Would expectation be that we would be sending him out on that? Carolyn, you hinted at this saying based on how well was he controlled at baseline? If he wasn't well controlled, it probably makes sense to keep him on that. But if maybe temporarily, we think he's going to have some more pain rather than discharge him with hydromorphone tablets on top of buprenorphine, what was the practice or what do you recommend to the audience about that transition of care when they're coming out of the hospital and they've been on short-acting opioids and then they've been on a higher dose of Bupe?

Carolyn: Yeah. And again, it really comes down to the clinical scenario for your discharge plan, and how severe the pain is, and what's going on clinically, how quickly do you expect them to improve. So, frequently, in my practice, I will discharge people on buprenorphine and full opioid agonists. For example, JJ, he has an epidural abscess. Let's say, he gets surgery, not very comfortable. He is going to have some continued pain likely in the postoperative setting. So, in that scenario, I'm leaving the buprenorphine dose where it is and then I generally taper the Dilaudid by one pill a day and just go from there.

Let's say, for example, JJ, he's on his buprenorphine and he was getting five doses of Dilaudid a day. Hopefully, over the next couple of days, he'll continue to improve. And then the great thing is since the buprenorphine is there, I don't have to worry about opioid withdrawal as I pull off the hydromorphone.

Matthew: Yeah.

Carolyn: I would say, he's getting it five times a day. Let's try breaking it down to four pills a day for the next couple of days, and three pills a day, then two pills a day, then one pill a day, and try and taper somebody off that way.

Matthew: If I were the primary care or the person prescribing his buprenorphine, I would definitely want to be in the loop about this because it just seems it's going to need very close follow up just to support the patient through that, decide if you need to prescribe any further short-acting pain control. Yeah, it's a tricky situation.

Carolyn: Totally.

Matthew: Again, it makes me nervous. That's why I'm glad to have you all here to answer these questions. Shawn?

Shawn: Yeah, I was going to say, I think as clinicians we have this tendency to overemphasize the harms we might do from doing something from the harms we might do from not doing something. So, discharging a guy who just had spinal surgery that's still using opioids in the hospital without any opioids and him having pain when he leaves the hospital enough so that he goes and starts using, that could destabilize him from OUD perspective, probably more than discharging him with a short taper that you're teaming up with his primary care doctor do.

I think it's always-- and this will probably come up later in the cases too. It's always worth thinking about that framework too have the harms of not doing something. I think for a lot of people that have these big surgeries, they do need tapers of short-acting opioids when they leave the hospital and partnering with hopefully some primary care friends and Bupe prescribers in the outpatient setting is going to be really helpful in that case.

Carolyn: Oh, when I write the scripts, as you said, partnership with the outpatient provider is key. This is the time where you pick up the phone, you send them a message. Generally, even if I think the taper is going to be for a prolonged period of time, I'm not necessarily writing a 30-day taper at discharge from the hospital because I think a patient just needs to be clinically reassessed. So, I'm really trying to send them out with what I think will be an adequate one week's worth of medications with a PCP follow up within that time or if it takes two weeks, then I will write for two weeks. But I really want to make sure 1, that they have that appointment set up and 2, as with any medication it needs to be reassessed within a short amount of time.

Matthew: Wonderful. Well, let's change the case a little bit. What if JJ had come in instead of being on buprenorphine for maintenance, he was on methadone maintenance, 100 milligrams, which from the wonderful Curbsiders Addiction Medicine episode I know, normal dose of methadone maintenance is 80 to 120 milligrams or a typical. I shouldn't say normal, typical dose. Shawn, what would differ about this same scenario JJ is coming in? He's got a thoracic epidural abscess. And so, he's got pain and we also want to keep him on maintenance therapy. How would you handle this methadone that he's on for maintenance and pain control?

Shawn: Yeah, I honestly think the framework that we talked about for buprenorphine still applies here. Methadone, an amazing medication for treating opioid use disorder, I think it's worth providing the context again, buprenorphine and methadone reduce mortality by 50%. These are some of the most amazing medications that we have in medicine at helping people live longer lives. But methadone just like buprenorphine, its effect on cravings can last up to a day or over a day, but its effect on pain is much more short acting. And so, same case of I would go to the person and ask, "How do you feel about splitting up your dose?" Sometimes, we find that for people that helps more with pain and think about splitting up their current dose into like TID dosing.

That being said, I think a lot of people, because the system that we provide methadone in this country is so rigid, they get very nervous about changing their doses around rightfully. And so, I always talk to people before splitting their dose up. And then same kind of thing if this guy's an epidural abscess, if he didn't have OUD, if he wasn't on methadone, you would use opioids to treat that pain. You should use opioids to treat this pain and just know you're going to have to use higher doses than typical, because they have a high tolerance. I don't think of as much of the delineation between having to use a higher affinity opioid, because methadone is not super high affinity. So, I think when people are on methadone, I still reach for oxycodone and things like that.

Carolyn: And even to add to that, which opioid do I select for that short-acting? I think it's good to remember that the neuroreceptor has just a ton of variability from person to person. So, some of my patients will be like, "No, this is the one. Morphine works for me every time or oxycodone works for me every time." So, go off what they tell you, if they have had positive and an effective analgesia from that. It's something to use. And also, if somebody is not achieving adequate analgesia on oxycodone or hydromorphone, it's okay to try an opioid rotation and just say, "Hey, this just seems to not be working for you. Let's just switch it up" and we may be able to get more relief. I have found that effective in a number of cases.

Matthew: I wanted to go back to the-- Is there any problems legally--? We're not going to discharge them on split-dose methadone, right? But if while they're in the hospital, are we allowed to give them 25 or 20 five times a day or whatever we need to do to make up a hundred. It's a little bit of a weird. I don't know if you can give 33 and a third three times a day or whatever. But how would you split that up and can we do that legally?

Shawn: Yeah. As per the regulations around methadone in the hospital are pretty much like any other medication in the hospital. You can essentially do whatever you want with it in the hospital. It's very regulated in the outpatient setting in terms of getting prescribed at an Opioid Treatment Program, which

is, again those kinds of, I don't want to call them clinics, but separate places where you go to get treated with methadone in the United States that are essentially removed from the healthcare system and we're done so on purpose. And so, in the hospital, you can use methadone however you want it. And so, just like methadone is used for pain in a split fashion, you can use it to split to try to help with pain when someone that's on it for OUD by splitting it up.

As far as the dose, I think it's very hospital dependent. Methadone comes in liquids and pills. And so, it'll depend on what's available at your hospital. But I think I have definitely split up into weird doses before and given someone like 33 milligrams [Matthew laughs] three times a day, probably the chagrin of a lot of pharmacists, but something that works.

Matthew: Okay. I like Carolyn. I like your approach. You told us with the first iteration of this where you would ask JJ, what do you want to do? Do you want to keep your dose the same? You want to make the pain treatment a completely different thing or do you want to try to split it up to see if that helps give you a little extra pain control and you're going to make full agonist opioids available either way to treat the acute pain part of things? The methadone is going to be continued for the cravings. And perioperatively, is methadone-- I don't know that I've ever asked this before. Is methadone any different methadone maintenance perioperatively? Is that something that the surgeons or the anesthesiologists don't like to have in the patient system?

Shawn: I have not come across that. I think anesthesia, there's some that use actually methadone in the operative setting to help reduce postoperative pain. But I don't think that I have not heard of any problems with it. I think it's worth addressing. There's a lot of stigma in the hospital in general. To go on a very brief rant too, I think one other expert opinion thing that I do is, I think people often get labeled as being seeking medications, is a term that's often used in the hospital because they have opioid use disorder and they have pain. And maybe they like Carolyn had said have identified an opioid that works for them often. And so, I think people's pain often gets ignored for that reason.

My expert opinion and personal practice is, I often schedule some opioids around the clock for people at the beginning or when I know what they're going to need for pain, so that they're getting assessed at a regular time interval. I'll schedule something like, say for instance, oxycodone 10 milligrams every four hours. When I expect they're going to need more than that 10 milligrams and have additional PRNs available, so someone has to check on their pain every four hours and then can give them the additional PRNs too.

Matthew: I like it. And I think the other thing that I just wanted to mention, because we talked about acute pain in the hospital with the great Dr. Melissa Weimer and she was mentioning just like adjuvant--We talked about thermal therapy, ice or heat. There're all sorts of adjuvant medications that we would be prescribing too. So, I don't want the audience to think that we're just saying everyone just opioids are all we're doing for this person's pain. That's just like the main focus of this show is how can we safely do this and how can we feel comfortable doing this. But we're all still going to treat the pain like we would anyone else's pain, multiple modalities. And so, I just wanted to mention that. But speaking of other things we're going to address, Carolyn, what else do you like to consider like patients

coming in the hospital with opioid use disorder and pain, insomnia, other symptoms like that? Can you speak to that a little bit?

Carolyn: There is a ton of things that can go into how we experience pain and hospitals are just really uncomfortable, unpleasant places to be. I think it's important to ask like, "How are you sleeping?" I know particularly for myself, when I do not sleep, I am grumpy and irritable. If I have an injury, it's worse. I think about adding a medication if folks are having trouble sleeping such as trazodone or Seroquel just to help with that, as well as managing underlying anxiety. It's really stressful for a lot of folks being in the hospital, particularly if they have a long hospital stay. So, I like to check in on this, see if they have an underlying generalized anxiety disorder that maybe warrants treatment or trying something as simple as just adding hydroxyzine just to help as well can go a long way. It's not going to fix everything by any means, but it can be really helpful.

Matthew: I want to spend some time on a little bit more of a complex case which is maybe, because I made it a little bit easier on this first one, although I still feel I learned a ton from talking through that with you. So, thank you. But now let's say that we had this same patient and this is I think everyone listening probably has this happen all the time if they're working in a hospital, where the patient's not on any medication for opioid use disorder, but they're coming in--

Let's just remind. So, JJ is 32. He uses 10 bags of IV fentanyl a day. He has only so far received 15 milligrams oxycodone that was started in the ER and the pain control is just not good and he's here with an epidural abscess. He's saying, "I'm going to leave if something's not done. I'm going to start to go into opioid withdrawal. This oxycodone is not touching my pain or my opioid cravings." So, how do you see the fact that he has fentanyl in his system? Maybe let's talk about that first Shawn. Why does this present a problem, if our goal is maybe to treat both the opioid cravings and the acute pain? Why is this such a complicated problem?

Shawn: Yeah, I think it's a complicated problem for a couple of reasons. I want to go on a brief rant before I get into the actual question to be honest if y'all are okay with that.

Matthew: Sure.

Shawn: I hate the framing that we always come across where people say, "Well, opioid withdrawal is not life-threatening and it's just a case of the flu." The minimization of how severe opioid withdrawal is, because truthfully, I've had the flu. I've not had opioid withdrawal before, but I've seen people in opioid withdrawal and it is way, way worse than the flu. It's bad enough that people because their opioid withdrawal is untreated choose to leave the hospital. When they've come to the hospital, which is a place that generally treats people who use drugs terribly, they leave the hospital despite having a life-threatening infection and then people who leave the hospital prematurely are more likely to die.

Opioid withdrawal is absolutely life-threatening if it leads to people prematurely discharging. Not addressing opioid withdrawal which this guy if he's not already in his impending is wise not the standard of care. It's medical malpractice in my mind. And so, back to the question that you asked probably five minutes ago, but why is the fentanyl in this guy's urine an issue? I think one is the drug supply is

incredibly variable right now, incredibly toxic, but it's incredibly potent too. And so, number one is this. If someone is using fentanyl, particularly if they're using IV fentanyl, they're probably going to have a very high tolerance for opioids. And so, you need to just take that into account coming in right at the beginning.

I think the other issue with fentanyl is that if his desire is eventually to get onto buprenorphine, what we know is that people who are regularly using fentanyl, it's just is a little bit harder to get them onto buprenorphine, it's a little bit higher risk of going into precipitated withdrawal. And so, that just comes into my calculations early on when I go meet this guy of, how do I get your pain under control, prevent withdrawal, first of all? And then in the long term, if you're interested in it, how do I get you onto the form of MOUD, the medication that you want to be on for opioid use disorder too?

Matthew: Carolyn, can you talk about why is fentanyl such a tricky thing compared to--? This is probably before my time, when patients were mostly using heroin, it was a 6 or 12-hour wait, then you could give them buprenorphine and precipitated withdrawal wasn't as much of a problem. Why is it a bigger problem with fentanyl?

Carolyn: What that means is basically if fentanyl, even though it's short-acting, it stores in folks' adipose cells and it has this protracted excretion back into the plasma. Even though it's short acting when you use it to IV essentially, it still lingers. If you have heavy irregular fentanyl use, it's storing in your cells and again it's making it hard to determine. One, is the optimal time to really start somebody on buprenorphine and in addition, like what Shawn said, the supply is super toxic. It's very variable. It's not just fentanyl. I sometimes like to think of them as high-potency synthetic opioids. So, we know there's a lot of fentanyl analogs that are out there that we don't fully understand what their chemical properties are and what the clinical implications are. I think the last bit of data I saw from direct checking was that about 75% of fentanyl tested really is fentanyl, but then another 25 of it is analogs and other high-potency opioids. So, that also comes to in the picture again making buprenorphine inductions more unpredictable.

Matthew: I want to bring in Shawn's analogy of this like speeding car, because I think we're going to talk about a couple of options here like what we can do. Buprenorphine is involved in at least two of the options. And then I see methadone or just full agonist opioids as the other two options. But Shawn, can you talk a little bit about these analogies to set this up? I think maybe we've mentioned it on the show before, but I think it always bears repeating.

Shawn: Well, I appreciate that you liked this analogy. The way that helped me understand what precipitated withdrawal is, although it's probably not the perfect analogy is, a car speeding down the road. And so, for someone that has full opioid agonists on their opioid receptors, and again, that can be any opioid, that can be oxycodone, prescribed things, that can be non-prescribed things, heroin or fentanyl, that's like a car going 120 miles an hour. Buprenorphine is a partial agonist as opioid receptor. So, it's like a car going very comfortable at 60 miles an hour. But we talked about buprenorphine has higher affinity at the opioid receptors. That means it grabs that receptor tighter. And so, if there are the other opioids on the receptor, because buprenorphine has a higher affinity, it wants to get on that receptor more, it kicks them off. And so, that's like the car again with the full opioid agonist is going 120

miles an hour, you give them buprenorphine, it kicks all of the opioids off the receptor, the car immediately slows to 60 miles an hour and that feels you're slamming on the brakes, and that's precipitated withdrawal.

I will say I have accidentally put people to precipitated withdrawal before from starting buprenorphine. I haven't done it commonly. Although it happens, it's more frequent. With people using fentanyl, it's still not happening every time we start buprenorphine, but it is horrible. People feel complete trash. They can barely move, they feel so terrible. And so, we should be trying to avoid it if we can and help people.

Carolyn: And we really should be trying to avoid it in patients who also have acute pain.

Matthew and Shawn: Yeah.

Carolyn: Because [laughs] ooh, yeah that person is not going to appreciate the medical care that they are receiving. So, it's a period of high risk. I'm really thinking thoughtfully about what is the best way to help this patient. And in addition, I do want to plug to that even though our supply has changed, MOUD like methadone and Bupe are still very effective for opioid use disorder. And there is data out there to suggest that it can still be used for treatment and there were some recent Canadian guidelines that stayed in their expert opinion. They're often recommending methadone doses greater than 100 milligrams for folks with regular fentanyl use. So, just because it's out there treatment is still very effective and we should be using it.

Matthew: Well, so, let's talk about this first scenario, which is let's say that maybe the pain is only mild and the patient says, "You know what, my pain is mild. I had fentanyl about four hours ago before I came to the hospital. I just want to try to make it and I want to try to get on buprenorphine." And let's take low dose initiation out of that. We'll talk about that next. What would be a typical way this person might get on to, if they hadn't received any opioids, this person has received opioids in the ER, so we got to wait at least 6 to 12 hours after that? But if they had used fentanyl, Carolyn, what would be a typical waiting period if we're going to put them on a 2 or 4 milligram dose or whatever dose we're going to use, a bigger dose of buprenorphine, not the low dose?

Carolyn: Yeah, in my practice and I'm practicing in the northeast, which I think does matter because the [unintelligible [00:35:59] is variable in different parts of the country. I'm generally waiting 24 hours or I'm encouraging people to wait as long as they possibly can to really try before they start the buprenorphine. I say it could be as early as 12. I think it'd be great if you could last 24 and if you can last longer than that that's okay. I am using higher doses these days. So, instead of giving 2 or 4 milligrams of buprenorphine, I am probably telling them to take either 8 or 12 right away and ramping it up quickly.

Matthew: Interesting. Yeah, because a lot of the pathways, places I've worked which is just a couple, they have a 2 to 4-milligram first dose for initiation, then you repeat it every two hours or something like that and max of 16 milligrams a day. This sounds like very quickly you might go up to 24 milligrams in the first day and you might be giving 8 milligrams every so often. That's different. Shawn, you were

going to say something? Is that similar to your practice now what Carolyn's doing the bigger dose wait as long as you can give a bigger dose?

Shawn: Yeah, I'll plug in for Curbsiders Addiction Med, where we did an OBOT episode with Christy Soran, who does a much better job of explaining the approach I think than I will ever do. But yeah, I essentially wait as long as I can. Things that I think about too is, if someone's going to be in the hospital for a longer period of time, there are times where I'll just give them some oxycodone for pain for a couple of days to push out withdrawal symptoms and let the fentanyl flush out of their system if it's not going to prolong their hospitalization and then just hold that for 12 hours overnight or something.

Matthew: Ah, that's a good idea.

Shawn: But that's something that I've just started doing. Yeah, I definitely push the doses. I'm giving at least 8 milligrams for the first dose. I think there are times where you just giving 16 for the first dose too and definitely for people that are using fentanyl, again, whatever is in the very toxic drug supply at this point and using it IV, I think it's pretty rare that they're going to stabilize on a dose that's less than 16 and probably are going to need up to 24. And so, I think ramping them up to 24 is the right way to do it.

The guidelines for how we started Bupe are still based on a lot of data in the pre-fentanyl area, I think and so, people are having to use their expert opinion and rapidly change to try to adjust and get people out of withdrawal as soon as possible and get them onto a therapeutic dose, so that they can engage in treatment.

Matthew: Yeah, and this is tricky in the hospital, because if the patient's in just mild pain and they're okay with waiting, you can wait or if they're in no pain and they're okay with waiting, then you can wait the 24 hours, give them some comfort medications for nausea, diarrhea, and anxiety, all those things. You can give them acetaminophen, or NSAIDs, or other things for pain. But what if it was more severe pain? Probably this is not the best option because the patient needs something now. So, do you want to talk about what are the options if the patient is in moderate to severe pain? I see there's maybe three, the low-dose initiation, methadone, or you give them just a full agonist. So, Shawn, maybe you go first. How do you decide between those options?

Shawn: Yeah. Just having a conversation with the person probably while they're getting some amount of opioids for pain and to hopefully prevent withdrawal symptoms, because truthfully, it's really hard to have a conversation when you feel like garbage from pain and withdrawal. And so, I think putting them on short-acting opioids and again using higher doses than you think someone without opioid tolerance would have, is going to be your first step, so you can actually have an informed conversation with them.

Matthew: Oxycodone 40 milligrams or 20, 30 milligrams, what is--? Usually, I start people at 5 or 10.

Shawn: Yeah. If someone is telling me and again this is getting some history, but if they're telling me that they're using fentanyl IV every day and they're using a bundle a day. But I admit that I'm probably starting underdosing and then ramping up, because you can always give more, you can't give less. And so, I'm often offering methadone first of all, as even if it's just like a pain withdrawal standard, kind of

just punch down the road for a little while, like put them on 30 milligrams of methadone, and then adding short-acting opioids, and starting them on standing. So, I started a lot of people in 15 q4 standing and then add additional PRNs and then I'm reevaluating.

Matthew: And the methadone is regardless of whether or not they're saying yes, I want to be connected with an outpatient methadone program, you're saying 30 of methadone just to get them feeling reasonably well from the opioid craving standpoint. That's not as much for pain and then you're going to give pain medicine on top of that?

Shawn: Yeah, I think it's both to help with withdrawal acknowledging that 30 milligrams of methadone is not going to make all of their withdrawal go away and not going to make their pain go away, but at least I feel it gives you a little bit of a baseline, but then you can add the short-acting on top of. I think if you're just using short-acting, you're just going to have to go usually with higher doses. And truthfully, I think using higher and higher doses makes a lot of people are uncomfortable. So, I think combining things can often just make it feel a little easier. But that's also based on patient preference too. I've definitely seen a lot of patients that don't even come near me with methadone, don't say the word methadone. In that case, I'm not going to give the 30 of methadone. I'm going to give them short-acting opioids and do what I can to get control of their symptoms quickly.

Matthew: So, Carolyn, if a patient didn't want to talk about methadone or buprenorphine, they said, "I'm here for pain. I don't want either one of those, I'm not ready for outpatient treatment, I just want to get my infection or whatever treated." Do you ever go the route of just giving full agonist opioids around the clock while they're there, Carolyn? What might that look like for you? I know this is not yet standardized everywhere.

Carolyn: Yeah, you should do it. Again, you should manage somebody's pain appropriately and just try and gauge them and meet them where they're at. And everybody deserves to have their pain treated while they're admitted in the hospital. Again, ideally, it'd be great to have an individual on methadone or buprenorphine because it actually often or means that they use less and lower doses of the full agonist. But if that's just not what they're interested in, it's totally reasonable to use full agonist generally. In my practice, I usually schedule short-acting, again ramp up pretty quickly and then adjust and go from there. It can be challenging to taper those medications long-term.

Occasionally, I will say, again, depending on how long someone's there, I may use a long-acting dose of OxyContin at night just because I think that short-acting is every three to four hours. When people sleep, it can be a little bit more challenging during that time. So, I will frequently schedule short acting during the day. I'll say, hold at night, if they're sleeping and give them a dose of long-acting full agonist opioids at the nighttime to help them sleep.

Matthew: Yeah.

Shawn: I want to say using short-acting opioids and addressing someone's pain in withdrawal is a way that you gain people's trust too. And so, I think not a lot of people have had the conversation of the true benefits of methadone and buprenorphine too. If you get someone stabilized on short-acting opioids in

the hospital while they're there, see they're getting treated for endocarditis, they're going to be here weeks, you can have conversations and maybe eventually figure out that maybe their goal is to get on MOUD at some point too.

Matthew: Right.

Shawn: And so, the door isn't closed just because when they're feeling like trash in the ED the first time they see you, they say no to. So, I think, again treating pain, treating withdrawal, this should be our standard of care to get people to treatment that they came to the hospital for.

Matthew: Yeah, and I hadn't considered the route of getting them on oxycodone or hydromorphone, whatever it is, oral and just treating them for a couple of days with that and then if they decide they do want to try buprenorphine, it's a little bit of an easier way to get them over. It's a little more of a predictable, we'll wait this long, you should be in enough withdrawal, we can put you on the buprenorphine. I guess, it's going to become the old-fashioned way, if the low-dose initiation thing becomes the standard. All right, so that's that.

To remind the audience, we're talking about scenarios where this patient is not yet on a medication for opioid use disorder, but he is coming in with both risk for withdrawal or at least mild withdrawal and moderate to severe pain. The first iteration we talked about as they had mild pain and we waited a long time, and then we put them on Bupe. But now we're talking about moderate to severe pain. We got to address the pain a little more quickly. What if the patient says they want to do methadone? Shawn, what might that look like? Would it still be the same 30 milligrams? If they're going to be there for a week, what might that look like and you're going to try to connect them to a methadone program when they leave?

Shawn: Yeah. And so, another pitch for Curbsiders Addiction Med, probably one of my favorite episodes with Dr. Ruth Potee. I hope I'm pronouncing that right-

Matthew: I think so. Yeah.

Shawn: -but she slammed the methadone episode out of the park. Honestly, it ramped me up. I got more excited about methadone. I didn't think I could be.

Matthew: [laughs]

Shawn: Just like buprenorphine in the era of fentanyl, in the era of this drug supply that we have, we know methadone initiations are adapting too. There was actually a really good article, I think it was by Zoe Weinstein out of BU recently. They're called for really, we need to do more research on how we initiate methadone, because the old way we did it, which was starting people on 30 milligrams of titrating by 10 milligrams every three to five days or every week is often too slow for people that are using regular fentanyl. And that period, when people start methadone is actually the highest risk period often for people. And so, in the hospital, someone's in a controlled setting, it's easy to give them 30 of methadone and again, using other full agonist to help with the pain and even to help with the withdrawal

symptoms, because we don't think that the 30 milligrams of methadone is going to cut it really for everything. And then you ramp up as you go.

For me, if someone is only using low levels of intranasal kind of substances, if they're only using pills like oxycodone prescribed things, I'll start at 20 or 30 and hold that there for a couple of days and slowly ramp up. If someone is using a lot of the illicit drug supply like fentanyl and the fentanyl analogs and using it IV, I'll ramp up quicker. And so, I do 30 on my first dose, I'll give another 10 that evening if they need it, and then I'll go up by 10 a day until we get to 70 on day four so, and then hold it at 70 for a couple days while using additional short-acting opioids for pain and withdrawal.

Matthew: Right, because the methadone, really we're using that for cravings, we're not necessarily-- I guess, we talked about, if someone was on a stable dose of methadone, we might split that up to try to work for pain control, but it seems like a safer thing in this case to just keep the methadone as the one chunk that you're given once a day, maybe an extra 10 and then you're using short-acting pain medicine to supplement that for the pain control. Okay, I like it. I think I'm getting this now. Carolyn, anything to add?

Carolyn: You can do either/or. I have kept folks split dose methadone when I'm initiating for pain purposes-

Matthew: Oh, okay.

Carolyn: -still with that again, overlying principle that we can add another 10 milligrams a day, I'll ask them where they want to add it. And another thing there sure is, if somebody does get a little bit sleepy later on, you can always hold the evening methadone dose. So, it depends what the patient needs.

Matthew: Okay.

Shawn: And I want to put a plug-in for, this is something where you need to know your community resources. There is a state, I honestly don't remember which one. There's a state in the United States that does not have any opioid treatment programs for methadone. And so, if you're in that state ramping someone's methadone up really quickly in the hospital's probably not the best thing to do, because you're going to have to figure out how to taper them off before they leave. And so, figure out or try to partner with some of the opioid treatment programs in the area, so that you can ramp up a dose in the hospital and then they can go to the opioid treatment program on that stabilized dose. If they leave the hospital on 70 or 80 milligrams and are able to continue the opioid treatment program after, that could be a humongous win towards keeping them on methadone.

Matthew: Yeah. Otherwise, probably, if the person was not going to get connected to a program, you'd be obligated to do some sort of a taper before they left the hospital.

Shawn: Yeah.

Matthew: Okay. With the last few minutes here, this low-dose initiation, Shawn, you wrote a paper with some of your colleagues about this. This low-dose initiation of buprenorphine, there're multiple protocols people have tried. Any of that you would recommend or how would you recommend people think about this? Is this ready for primetime yet or is this something that people should hold off on?

Shawn: I think it's ready for primetime in certain clinical situations. In most clinical situations, especially in like the clinic and things like that I'm still going for whatever we're going to call it, our traditional or old school Bupe initiation where we're having them stop for a day, wait for withdrawal symptoms, and then starting buprenorphine. Low-dose initiation of buprenorphine which goes by a lot of names also rapid overlap initiation of buprenorphine, the term micro-dosing was used previously, although I think it's not the most accurate term and so, I tend to avoid it. But the way that it works is essentially you're taking really small doses of buprenorphine while someone is still on whatever full opioid agonist they're on and very slowly ramping up the dose over the course of days.

Going back to our car analogy, if someone says, this guy is in the hospital now, we've treated his pain, he's gotten through his surgery, his pain has stabilized, he's in a good spot, he's just waiting to have safe placement to continue his six weeks of IV antibiotics for his endocarditis, or osteo, or something, and he's on oxycodone 15 q4 and has been on that for a couple of days to help his pain and withdrawal. In that case, he's got full opioid agonist on his receptors, the car is going 120 miles an hour, but we don't want to just stop his opioids because he still has pain from the surgery and going through withdrawal for 12 hours and acute pain is just not a reasonable thing for him at this point.

We start really tiny doses of buprenorphine. On day one, we start 0.5 milligrams, day two, we go up to 0.5 milligrams twice a day. And each day, a little bit of the buprenorphine displaces the full opioid receptor on the agonist. And so, that car that was going at 120 miles an hour on the oxycodone on day two, when there's also 0.5 milligrams of buprenorphine, the system is now going 110 miles an hour. And the next day, we go up on the Bupe a little bit more, a little more Bupe displaces the opioids and the car slows down a little bit. Until we get them to a therapeutic dose on day five, six, seven and then we can stop the opioids because all their receptors in their brain have buprenorphine on it and the car had never really had to have an abrupt stop and so that person never went into withdrawal.

Matthew: I love it. It's like gradually hitting the brakes on the car.

Shawn: Yeah.

Matthew: Yeah. It's beautiful. Potentially, the patient just doesn't have to go through any withdrawal symptoms at all. You avoid this whole risk of precipitating withdrawal or the patient just having to feel miserable for 24 hours while you're waiting for everything to get out of their system.

Shawn: I'll say this is still relatively in the realm of expert opinion. All of the literature on low-dose initiation of buprenorphine is all case reports and case series and retrospective chart reviews and things like that. There are definitely some principles that you can glean from it. There's a lot of different protocols that you can use. In the hospital, it's going to depend on what buprenorphine formulation you have in the pharmacy because you have to get to those doses that are below the strength of the lowest

strip or tab, which is 2 milligrams. And so, in some hospitals, you have to use IV buprenorphine, some you can use the buccal or buccal, I never know how to pronounce that word, formulation of buprenorphine.

Matthew: [laughs]

Shawn: Some hospitals let you split up the films, but what you really need to do is continue the full agonist throughout the entire time that you're doing this transition, because if you start tapering their full agonist or stop their full agonist, they're going to go into withdrawal and then you're not going to know if it's from the buprenorphine or from the full agonist. And so, continue the full agonist, slowly increase the Bupe dose, and then when you get to therapeutic like 16 milligrams, you can stop the full agonist.

Matthew: Yeah, I've even seen some patients, I know there's some protocols out there. Maybe the patients even on hydromorphone PCA and then you start doing the buccal buprenorphine gradually building up their dose. And so, just whatever they need for their acute pain control, they're using that. I guess in the outpatient scenario with this, they might still be whatever fentanyl they're illicitly using, they would keep using that as you ramped up the buprenorphine. Carolyn, in the hospital, anything to add to this final scenario that we're talking about with this low-dose initiation?

Carolyn: I think exactly what you said. Make sure you're scheduling the full agonist. I definitely have seen folks run into some issues if it's PRN, because it's really important to keep that medication on and keep those receptors saturated with therapy-signed opioids. I also think that sometimes it definitely decreases your risk of having any precipitated withdrawal. Occasionally, some patients may experience a little bit of minor discomfort. So, I do counsel patients on that at the start just so they're prepared. We think that this is really going to help make this transition much more smooth for you in terms of getting onto buprenorphine. If at any point you're having discomfort, please let us know. We want to make adjustments. We may need to address the full agonist or give comfort medications, but we just want to keep an open line of communication, so we can help treat and manage symptoms as they go through that process.

Matthew: We talked about the hard way to get on a buprenorphine is like you wait a really long time and then nowadays a bigger dose, 8 milligrams, 12 milligrams of buprenorphine after that long wait. If we do precipitate withdrawal, how are you handling that and should we just give them back full agonist opioids to try to pull them out of withdrawal? Would that even work? What's the approach there?

Shawn: Yeah. Precipitated withdrawal is still this-- It always brings up so much anxiety in me. I'm not even the one experiencing it. I think it depends on the context. My thoughts are it depends on the context of the precipitated withdrawal. If you're doing a traditional initiation where you just gave someone whatever, 2, 4, or 8 milligrams of buprenorphine, I think the literature is mostly case reports and how to treat this, but most of the literature suggests you give more buprenorphine and you give all the other medications you can for comfort. You're giving like clonidine, which we know has data that it helps with opioid withdrawal, you're giving NSAIDs, you're giving loperamide to help with diarrhea, you're giving everything you can to help them feel better. That includes benzodiazepines, right? Precipitated withdrawal is horrible. People have horrible anxiety and feel terrible during it. It's okay to

give benzodiazepines especially in the hospital. There is a little bit of case reports on ketamine and precipitated withdrawal. That'll depend on your comfort level and your hospital's regulations on who can use ketamine to be honest.

Matthew: I'll wait on that one. [laughs] Okay.

Shawn: If you're doing a low dose though and someone start-- I've never had someone truly precipitate during a low dose. I don't know, if you have Carolyn. But I've had people that have mild opioid withdrawal symptoms during it. In that case, I'm maybe slowing down the low-dose initiation a little bit., like slowing down how quickly I ramp up the dose, taking a pause at that dose, or using additional comfort meds. I think it can't be said enough like, this should be patient-centered. And so, talking with them through the process, and what makes them comfortable about going, and what do they think a good next step is to.

Carolyn: I think I have had a scenario where I thought it was truly mild precipitate withdrawal and I just gave an extra dose of a short-acting opioid and they did pretty well.

Matthew: Okay. Well, we've talked a lot. I think this will probably be covered on future episodes again as we have more information to update this. People should definitely check out all the Curbsiders Addiction Medicine episodes with Carolyn, and Shawn, and friends. Let me ask Carolyn and Shawn, did you each have one or two take home points you wanted to give? Carolyn, we'll start with you.

Carolyn: I think all my take home points are Shawn's rants.

[laughter]

Carolyn: I don’t feel that we can just put those in the notes. I'm trying to remember what his first one was. I think the one most recently is, we must absolutely treat opioid withdrawal. It is a medical emergency to treat opioid withdrawal. We must do it. We have many tools. We can use methadone, buprenorphine, full opioid agonists. Whatever you choose, we have to treat it and we have to treat it aggressively. And in addition, if you're on MOUD, you can still treat pain with full agonists. Keep them on their Bupe, keep them on their methadone, and then just add the full agonist on top to help patients be successful in both their pain management and their OUD.

Matthew: And Shawn?

Shawn: Yeah, I don't know if I could say-- I think you said my rants better than I did, Carolyn. Yeah, I think the biggest take home for me is, yeah, trust your patience. If they're saying they're in pain, if they're saying they're an opioid withdrawal, they're probably in pain and they're probably in opioid withdrawal and treat it like-- Don't overemphasize the risk of accidentally giving someone opioids to the risk of not treating someone's pain and withdrawal and then do not stop their medications for opioid use disorder. There're almost no circumstances where you should stop someone's buprenorphine and methadone when they're coming in for pain, or coming in for withdrawal, or something like that.

Carolyn: I have one more to add. Don't use the term drug seeking, [unintelligible [00:58:38].

Shawn: Yeah.

Carolyn: I think we can all do better. We can avoid that term and it's stigmatizing and really is not accurate and not helpful.

Matthew: All right, thank you both.

This has been another episode of The Curbsiders bringing you a little knowledge food for your brain hole. You can get show notes at *thecurbsiders.com*. You can also get transcripts and sign up for our mailing list to get our weekly show notes in your inbox, plus twice each month you'll get The Curbsiders Digest, which recaps the latest practice-changing articles, guidelines, and news in Internal Medicine. We're committed to high-value practice-changing knowledge. So, we want your feedback. Please subscribe, rate, and review the show on Apple Podcasts or on Spotify. You can also email us at *askcurbsiders@gmail.com.*

A reminder that this and most episodes are available for free CME through VCU Health at *curbsiders.vcuhealth.org*. I wanted to give a special thanks to PodPaste who helps to produce and edit the show. Elizabeth Proto runs our social media. Stuart Brigham composed our theme music. And with all that without Dr. Paul Nelson Williams, until next time, I've been Dr. Matthew Frank Watto. Thank you and good night.

[music]

[Transcript provided by SpeechDocs Podcast Transcription]