

## RESCUE MEDICATION DELIVERY METHODS AND FUTURE THERAPIES

- Laura Lubbers: [00:00](#) Welcome everyone to today's webinar. I'm Laura Lubbers, and I'm the Chief Scientific Officer for Citizens United for Research in Epilepsy, or CURE. Today's webinar is entitled Rescue Medication Delivery Methods and Future Therapies, and it will be presented by Dr. Nathan Fountain. This is a second installment of a two-part webinar series that describes seizure emergencies, reviews available rescue medications, and describes those in development. Today's webinar is being sponsored by our friends at the BAND Foundation.
- Laura Lubbers: [00:34](#) CURE's mission is to find a cure for epilepsy by promoting and funding patient-focused research. CURE's robust grants portfolio has advanced epilepsy research across areas such as infantile spasms, post-traumatic epilepsy, sudden unexpected death in epilepsy, or SUDEP, and epilepsy genetics.
- Laura Lubbers: [00:55](#) Dr. Fountain, who is our speaker today, is the Thomas Worrell Professor of Neurology and Epileptology at the University of Virginia where he is the Director of the Comprehensive Epilepsy Program. He is the President of the National Association of Epilepsy Centers and the Chair of the FDA Advisory Committee for Nervous System Drugs. He also performs clinical research to test potential new drugs and devices to treat epilepsy.
- Laura Lubbers: [01:22](#) Before Dr. Fountain begins, I want to encourage everyone to ask questions. You may submit your questions anytime during the presentation by typing them into the Q&A tab located at the bottom of your Zoom panel and clicking Send. My colleague from CURE, Brandon Laughlin, will read them aloud during the Q&A portion of the webinar.
- Laura Lubbers: [01:42](#) We do want this webinar to be as interactive and as informative as possible. But to respect everyone's privacy, we ask that you make your questions general and not specific to a loved one's epilepsy. So with that, I'll turn it over to Dr. Fountain.

Dr. Nathan Fountain: [01:59](#) Thank you very much, and thank you for inviting me to speak today. I hope we're able to cover a lot of things that everyone finds useful. It's a really exciting, new time to talk about rescue therapies and what I might call, abortive therapies.

Dr. Nathan Fountain: [02:17](#) The topic today is very timely. Before I begin though, I want to talk about why it's timely because there's so much research going on and talk about my disclosures. I do a lot of clinical research, as we mentioned, sponsored by these companies listed here, some of whom have developed rescue therapies, particularly Neurelis, Engage, and UCB.

Dr. Nathan Fountain: [02:43](#) I'm going to talk about the off label use of many medications. That means they use these medications for things that are not approved by the FDA. Physicians often prescribe medications, particularly in the epilepsy space, for things that are not particularly indicated, and I'll try to talk about that but I want you to be aware of that. In particular, I'm going to talk about medications that are in development which are not available now, and of course, since they're not available now, are not FDA approved.

Dr. Nathan Fountain: [03:09](#) I also want to really emphasize before I begin that all these treatments can cause serious side effects or problems, so all aspects should be discussed with your physician. Of course, seizure emergencies are seizure emergencies by definition so we use stronger, powerful medications to treat it, and consequently the medicines themselves can have problems. So, it's really important to discuss all of that with your physician.

Dr. Nathan Fountain: [03:33](#) So, moving to what we're actually going to discuss. We're going to talk about what are seizure emergencies? You know exactly what we're talking about, and that's more complicated than it might seem. We're going to talk about when a rescue medication is used, what is the history of rescue therapies because right now we're in a big transition from sort of a long historical lag to what, probably, is about to be an explosion in rescue therapies, who should have rescue therapies, which has kind of a short answer, and what rescue medications are

available now, and that's really what we'll spend most the time talking about because it's probably what you want to know most, if you or your loved one has epilepsy you want to know what's available now.

Dr. Nathan Fountain:

[04:09](#) But also, we want to talk about what rescue medications are in development because that's also important because some of those will be available soon. So, what is a seizure emergency? Well, to talk about that we have to back up a little bit and provide some definitions so we know exactly what we're talking about.

Dr. Nathan Fountain:

[04:25](#) So, what is a seizure? Well, a seizure is an event of altered movement, or behavior, or thinking. In other words, someone does something that's due to sudden discharges of nerve cells, or neurons, in the brain. So that means the brain's ticking along normally, has this electrical storm that goes on for a while and causes a seizure, and then stops.

Dr. Nathan Fountain:

[04:43](#) Epilepsy on the other hand, is the actual underlying condition that gives the tendency to seizures or the tendency to spontaneous, recurrent seizures. So in other words, seizures that come out of the blue although they might be provoked by something. So, it's the underlying condition. So, those are things that are kind of in the background.

Dr. Nathan Fountain:

[05:01](#) So now let's talk about clusters. Almost everyone with epilepsy who has had even more than a few seizures will think about their seizures in terms of clusters. A cluster is just an increase in seizure frequency. For your cluster, you have a clear definition in your mind. Well, of course, it had more than usual. For me, if I have one seizure a month and I had one a day for three days, that's a cluster of them.

Dr. Nathan Fountain:

[05:23](#) On the other hand, if I have seizures every day and one day I have 20 of them, that's a cluster of them, but those are really different things because one seizure once a day for three days is a discrete event, which pretty much you fully recover for instance, whereas you have many in one day, you might not recover between them or you might have a different urgency in treating them.

Dr. Nathan Fountain: [05:41](#) So, clusters has individual meaning that's clear to each individual, but it's not clear in general. Another term for it is acute repetitive seizures. That's the term that historically the FDA has used or at least has been used in FDA applications for drugs we'll talk about like rectal, diazepam or Diastat. This is an increase in the number of seizures typically within one day and usually over the course of minutes or hours.

Dr. Nathan Fountain: [06:07](#) So, it's acute repetitive seizures. That's to be distinguished from a prolonged seizure, which is a single seizure that lasts more than five minutes, but less than 30 minutes. We'll talk about why that is shortly.

Dr. Nathan Fountain: [06:19](#) So, a prolonged seizure, one long seizure, is to be distinguished from a number of brief seizures that occur over a short period of time, and that's to be distinguished from a number of seizures that happen over say days, even though that might be many more seizures than you normally have.

Dr. Nathan Fountain: [06:33](#) Finally, there's status epilepticus. Status epilepticus is one long seizure that lasts more than 30 minutes or a number of seizures over the course of 30 minutes in which you don't wake up in between, and so might have ongoing brain seizure activity, even if you're not having, say, jerking or other behavioral manifestations of the seizure.

Dr. Nathan Fountain: [06:52](#) The reason we distinguish status epilepticus from just a prolonged seizure is because if a seizure goes on for more than about 30 minutes, it's unlikely to stop spontaneously. So, it requires intervention. It also can cause lots of other problems. Not surprisingly one long seizure can lead to even death. So, we distinguish status epilepticus from a prolonged seizure, from a brief seizure, which we just kind of arbitrarily call five minutes.

Dr. Nathan Fountain: [07:15](#) And when I say, arbitrarily, that's not quite right because most seizures stop within five minutes. If they don't, and they go on to 30 minutes, there's some reasonable chance they'll go on even longer than that. So as we think about seizure emergencies here, we have to think about the timeframe or which they occur because they have different kinds of urgency

and therefore you can imagine would require different kinds of treatment.

Dr. Nathan Fountain:

[07:39](#) So that means when are rescue medications used is a next logical question. These are also called a board of therapies, which I personally prefer to rescue medicines because I think of rescue is someone hanging over the precipice and you can go bring it back to the precipice and then treat whatever's wrong with them. Whereas a board of therapies means you're going to stop the seizure no matter what, even if you don't save them in any other way. But so it's entirely arbitrary, I personally prefer abortive but in generally, they're called rescue medications now.

Dr. Nathan Fountain:

[08:08](#) One good thing about calling rescue medications it does convey the urgency that generally is required. This refers to use of medicines at home, or at least not in the hospital by patients themselves or by caregivers. So non-medically trained personnel and it has several uses. Now that we've talked about the kinds of seizures, we can talk about the kind of uses.

Dr. Nathan Fountain:

[08:29](#) So first of all is to stop an ongoing prolonged seizure or to prevent the next seizure. So, you have one seizure when you have a cluster of seizures or even one seizure, you know you're going to have more, so you want to stop the next seizure, that's important. Or, stop the current seizure from progressing. This is something we don't talk about much, but can happen. So, some people who have seizures have a very small seizure, an aura let's say, or have just a few jerks that ultimately can culminate in a big convulsive seizure or some bigger seizure.

Dr. Nathan Fountain:

[08:58](#) So by taking an abortive medicine or rescue medication, it might stop the seizure from progressing. So, these are three different kinds of situations that we have to consider when you think about this. That requires thinking a little bit about the history of the therapies because historically, we only thought about prolonged seizures. We didn't really divide the set much into those other categories. It's important to recognize that as we talk about how we thought about it.

Dr. Nathan Fountain: [09:25](#) So, if we go back to before the year 2000, the advice given was to call the rescue squad. And even in the rescue squad, there's pretty limited intravenous IV therapies that the EMS, the Emergency Medical Services, would give. So for instance, when I was a medical student or early in training, I had one mentor who said to me the first thing to do if somebody is having a seizure is, "Go get a cup of coffee," because most seizures stop on their own. That's what he meant by that. But it was also true.

Dr. Nathan Fountain: [09:53](#) If we go back 30 years, we didn't really have much to stop a seizure with. That was kind of the underlying philosophy and the other underlying philosophy all those years ago, before 2000, was really that seizures were unlikely to do harm unless they were very prolonged. So, you got to think of that in the background, as you think about where we're at today. We did have some off-label use of IV forms of diazepam, for instance, which could be injected rectally.

Dr. Nathan Fountain: [10:19](#) So, if we go back to even the late 1980s, there were a few neurologists who were specialists in epilepsy that would prescribe the IV form intravenous form of diazepam that comes in a bottle that could be pulled into a syringe and injected into the rectum from the syringe without a needle. That had lots of issues with it. You can imagine the main issue is you can't just go to the pharmacy, your regular outpatient pharmacy, and order up IV medication, strictly not back then.

Dr. Nathan Fountain: [10:45](#) There's really limited prescriptions, even for oral pill forms of these medicines that we use now, like diazepam or lorazepam, and clonazepam. So for example, before 2000, it was pretty rare to give someone a prescription to say, "Take this pill. If you have two seizures in one day, take this pill to prevent the additional seizures in that day." That didn't happen very often. So now if we go ahead to the next area, which is between about 2000, 2010, rectal diazepam was approved and the brand name of that is Diastat. That was approved in 1997.

Dr. Nathan Fountain: [11:19](#) At that time, there was kind of a limited, but growing use of oral pill forms because with the

approval of Diastat became recognized that really we should be treating these kinds of seizure emergencies as an outpatient. There's also increasing recognition that that was safe because the concern all along is that it would be unsafe that these medicines would cause people to stop breathing or for their blood pressure to go too low.

Dr. Nathan Fountain: [11:42](#) Then if we move ahead to the 2010s to now, to today, we really see an increasing oral pill form and rectal diazepam use. So, it's much more common now than ever before. We also see a lot more now off label use of other IV forms of midazolam. So in the past 10 years, midazolam has become more popular. We'll talk a little bit about that. That's because it can be given intramuscularly into a muscle, which if you're familiar is a relatively simple thing to do.

Dr. Nathan Fountain: [12:11](#) Now recognize people who are not medically trained, that seems intimidating, but it's relatively simple for anyone with even a little bit of medical training. We also have increasing use of intranasal, so up the nose forms of medications, which were pretty uncommon until the past 10 years, even in a medical setting.

Dr. Nathan Fountain: [12:29](#) Now in a medical setting, for instance, anesthesiologists often use intranasal delivery of drugs for children who, of course, don't want to get an IV just like everybody else, but especially more than everybody else. That has spread also outside of the hospital to use at home as an off-label use of this.

Dr. Nathan Fountain: [12:49](#) Now, we have to talk about what rescue medications are approved for use to start with. In other words, where are we starting from today? What's available today before we talk about what will be available in the future. The kinds of medications we use are benzodiazepines.

Dr. Nathan Fountain: [13:05](#) Benzodiazepines are whole class of medications that are commonly used in medicine, have been around for a long time and are familiar to physicians and to a lot of people at home too, of course. Diazepam is a generic name. So, the chemical name for drugs you might be familiar with like Valium or Diastat is the rectal form of diazepam.

Dr. Nathan Fountain:

[13:24](#) Lorazepam is a different benzodiazepine and that's the generic or chemical name for Ativan, to which you might be familiar. So, it's often called Ativan instead of lorazepam and clonazepam whose brand name is Klonopin. Clonazepam is somewhat commonly used for the regular outpatient treatment of epilepsy, unlike the others. So, it's something that's sometimes prescribed for everyday use to prevent seizures, unlike these others that we're talking about that are taken just when you have a cluster of seizures or acute repetitive seizures or a prolonged seizure.

Dr. Nathan Fountain:

[13:56](#) Then Midazolam or Versed. Midazolam until now has really had no outpatient uses. It's something that is used in the hospital under tight control, because it's relatively powerful. What's meant by powerful, which isn't really a medical term of course, is that it's potent. That means a little bit of it goes a long way. So in the hospital, we're very careful about how we give that intravenous or IV form of midazolam. So, if it gets too much, it'll put someone right to sleep and could even suppress their respirations. So, we're very careful to use it.

Dr. Nathan Fountain:

[14:28](#) It has that history or background. But in relatively small doses, it's safe as we'll talk about. Then alprazolam, which is commonly known as Xanax. For most people with epilepsy they're probably cocking their head saying, "Xanax for epilepsy?" It's true that we have not used alprazolam or Xanax commonly as a rescue or a board of therapy for seizures. There's a number of reasons for that.

Dr. Nathan Fountain:

[14:49](#) One is it's very short acting, but also we're just not familiar. So, that is not been popular. But the reason I'm talking about it is because a different form, an inhaled form is in development as a rescue therapy. The common thing that all of these drugs do is inhibit brain nerve cells from firing. So, they work on the GABA system, the G-A-B-A system. The GABA system is what inhibits your neurons, keeps them from firing.

Dr. Nathan Fountain:

[15:16](#) So you can imagine if the seizure's too much firing neurons, and if you shut that down, it'll stop the seizure. That's pretty fundamentally the way it works. In medium doses, these can be sedative. So, as I

mentioned for midazolam, that you might know as Versed, we use it in the emergency room or in the hospital as a mild sedative. That is when someone needs a little bit of anesthesia. But in high doses, all of these can slow or stop breathing. They make people unconscious. So, you can use them as anesthesia in high doses.

Dr. Nathan Fountain:

[15:45](#) But the reason that's a risk or what the concern is, is that it can stop someone's breathing. The IV forms are very effective at stopping ongoing seizures in the emergency room and in the emergency room, it's a tight controlled situation. So if someone stops breathing, we have all kinds of mechanisms to take care of it. Although the outpatient home treatment of seizure clusters or acute repetitive seizures, it's something new to think about. As an inpatient, in the emergency room, it's established care. It happens every day and we don't give it a second thought. So, these medicines are used in the ER every day without any concern, because everyone's familiar and have established protocols or ways of doing that.

Dr. Nathan Fountain:

[16:29](#) The formulation for rescue medications is really important. That means the way in which it's made up, because remember, you could take a pill, everybody's familiar with that. You could use it as an IV form that goes in a vein, you're familiar with that. We talked about the intramuscular form in which is injected into a muscle. So think about it going into a big thigh muscle, for instance, or a shoulder muscle like when you get a vaccine, sometimes you might think about as an intramuscular form.

Dr. Nathan Fountain:

[16:55](#) But there's other places you're less familiar. It can go into the rectum. So that's rectal medication that goes into the bottom and that's absorbed somewhat easily. Not surprisingly when you think about that soft mucosal lining, meaning the lining of the rectum, and then it can go up the nose. So, that's intranasal. We can think about that with things like Afrin.

Dr. Nathan Fountain:

[17:16](#) When you have a bottle, you squirt up your nose and then it gets atomized. It gets turned into a very fine mist that deposits itself in the nasal epithelium, that's the lining of the nose and it's

absorbed easily that way. So, the formulations that are available are really important. They're listed here on the slide for each one of the drugs.

Dr. Nathan Fountain:

[17:35](#) Diazepam, that is Valium, the thing that most people are familiar with comes in a pill form, of course. That's what usually you're thinking about. It can also be given rectally as a gel and that we'll talk a bit about or it can be given IV whereas lorazepam is only available in the pill form or the IV form. It's not available on gel. It's not intended to be dissolved under the tongue, but it is possible to do.

Dr. Nathan Fountain:

[17:58](#) So, some people put lorazepam pill under the tongue and it can be absorbed. There's a number of problems with that. The most practical, simple problem is that it's probably not going to stay under the time and some forms, particularly generic form doesn't dissolve very well. It's probably most often just gets dissolved in the saliva and swallowed, but there may be some increased absorption to put under the tongue.

Dr. Nathan Fountain:

[18:21](#) Clonazepam also comes in pill form, and that's the only form it comes in, in the United States. It can be available as a wafer. You can put under your tongue, that's a little bit difficult to get, but it's available. So most people just use a regular clonazepam pill. The wafer historically has only been available in brand name. That's a little expensive and complicated.

Dr. Nathan Fountain:

[18:42](#) Midazolam or Versed in the popular brand comes in an IV form, an intramuscular form, that we've used for a long time. That same IV form can be given intranasally. So, it's possible to simply get a bottle of the IV medication to draw it up in a syringe, to put an atomizer, the little thing that turns into a mist and blow it up the nose.

Dr. Nathan Fountain:

[19:05](#) As a matter of fact, you can do that with any medicine that's mixed in water or something like water. The problem is sort of two or three fold. So, the first problem is it's a pretty big volume. So you have to blow a lot up the nose, like a whole milliliter, which you can think of as a sort of a fifth of a tablespoon or a teaspoon. So, it's a pretty big volume to put up your

nose. It's not a very big volume to swallow. You can swallow a milliliter easily, but when you're blowing up your nose, it's kind of a lot of it.

Dr. Nathan Fountain:

[19:35](#) The second problem is that when it's atomized, do you want these little atomizers that you force through? It's not necessarily atomized, so not all of it goes up. Some just get squirted and it gets squirted at the back of the nose. It'll just be swallowed. The third problem is you have to know that even if it gets deposited on the nasal epithelium, that is the nasal mucosa, the lining of the nose and the passages it's actually going to be absorbed. So, it's a little more complicated in just squirting something up the nose. That's why it's taken so long to develop the intranasal forms. It's also a little difficult for pharmacies because a lot of them don't like to distribute medications that are intravenous and tend to be intravenous to people for home use.

Dr. Nathan Fountain:

[20:18](#) But nevertheless, it's increasingly popular. I've certainly prescribed it many times. So, who should have rescue therapies? Well, anyone that needs to stop an ongoing prolonged seizure. The important thing about this is that the person's not aware. You have to avoid oral medications that is medicines given by mouth. And there's two reasons.

Dr. Nathan Fountain:

[20:38](#) The main reason because you don't have to choke on the pill and have to have any ongoing seizures, you're probably not able to get it in their mouth in a way they can swallow anyway, particularly the big convulsive seizure. So, you have to think of other ways to give the medication. You also want a medication that's going to act quickly because of course you want to stop that ongoing seizure quickly.

Dr. Nathan Fountain:

[20:56](#) If the medicine doesn't kick in for half an hour, then they're going to be seizing for half an hour before it works. You want something that works quickly. So, that's important for ongoing seizure treatment. Then if you think about, you also may want to take it to prevent the next seizure. That means, you know you're going to have a cluster and you're going to prevent the next one, a cluster. So, I gave two examples earlier.

Dr. Nathan Fountain:

[21:12](#) One, I said, one person has a cluster. One seizure day for three days, let's say it's a woman around her menstrual period. So, she knows that she has one today, she could have one tomorrow. Well, in that circumstance, you can simply take a pill. It doesn't kick in for a long time, as long as it works for a whole day for instance.

Dr. Nathan Fountain:

[21:28](#) On the other hand, for someone who has seizures, let's say once a day, but occasionally when they have two seizures, and you know they're almost always going to go on to have 10 seizures, and therefore they want to prevent the next seizure in the next few minutes. Then you need a medication that can kick in very rapidly. You also might need a medication that's not oral because maybe to get it right after that first or second seizure before the person's awake.

Dr. Nathan Fountain:

[21:49](#) So that has important implications for the kind of medicine or form of the medicine that you're going to give. Because if they're awake and swallowing, then you can give the oral medication. And it works a long time, you can use a pill, but in most circumstances, you'd like to do some other formulation. Finally, to stop the current seizure from becoming more severe. So imagine someone has auras, or still have a funny feeling in their head. They have strange sensations. Now, that goes on for say 30 seconds or a minute before it goes on until they're unaware. Then maybe secondarily generalized a big convulsion.

Dr. Nathan Fountain:

[22:19](#) So, you want to stop that as soon as it starts, let's say, or if somebody has a few jerks, they know that when they have a few shoulder jerks, but then over the next few minutes, it's going to get bigger and culminate. So, they want to take something right away to stop it. That's more or less the same thing as stopping a prolonged seizure, except often people are awake and alert interactive so they can participate in whatever you're going to give them. That's an important distinction.

Dr. Nathan Fountain:

[22:43](#) So, who should have rescue therapies? Well, not necessarily everyone, but all people with seizures should have a seizure action plan. Seizure action

plans can be very simple or very elaborate. All schools in Virginia, for instance, where I practice, require a formal seizure action plan. It's a document that's written out that says, "Here's a description of a seizure. Here's a normal seizure. Here's what to do normally. Here's what to do for a prolonged seizure. Here's exactly how much medicine to give and how much to give it."

Dr. Nathan Fountain:

[23:12](#) For people who have seizures frequently, it's important to have a seizure action plan just like that, whether they're in school or at home or anywhere else, because you want to know that in those cases, when there is something that's prolonged or different, that there's an action. But there is another end of the spectrum. So, imagine people who've only had one or two seizures had just been diagnosed with epilepsy or somebody who has infrequent seizures once every few months or six months, or once a year. Those people don't necessarily get the same of seizure action plan, but they need an action plan sort of in concept.

Dr. Nathan Fountain:

[23:49](#) So, they need to know that in the unusual situation of a prolonged seizure, or even the occurrence of one seizure, for instance, if you have newly diagnosed epilepsy, what to do. What to do is probably not give them one of these rescue therapies because they probably don't need it because their seizure's probably going to stop on its own. So in that case, the seizure action plan is simply to tell the people around you, that if you have a seizure, you need to call the rescue squad, you need to go to the ER to find out why you had the seizure and what needs to happen next?

Dr. Nathan Fountain:

[24:14](#) So, everyone with epilepsy needs a seizure action plan. Anyone who is at risk of any of these kinds of things I've talked about, their seizure action plan needs to include a rescue therapy. As I mentioned, historically, the rescue therapy was call the rescue squad. So another aspect of living in Virginia is it's very rural. I'm in Charlottesville, Virginia, where the entire population is about 100,000 people in the entire county. So on average, my patients travel a couple of hours to get to see me and I have a clinic five hours away, as a matter of fact.

Dr. Nathan Fountain:

[24:43](#) So, we have people who live in very rural areas. If you live in a rural area, it might take the rescue squad quite a while to get there. So not only for medical reasons, but also for peace of mind in those situations, I personally very frequently prescribe rescue medications to almost everybody who's at any risk of these things. If we look at the big picture, about 18% of people with epilepsy, so about a fifth of people with epilepsy will have a prolonged seizure at some time long enough to be called status epilepticus.

Dr. Nathan Fountain:

[25:12](#) Overall, about a fifth of people with epilepsy will have this. That means about a fifth of people with epilepsy at least should have a rescue medication plan. So, discuss it with your doctor and make a plan is the key. If we consider the aspects of rescue medications that we would use in selecting a rescue medication, we first have to on this recurrent theme, is it to stop a seizure? Is it to prevent the next one? Are they likely to have a level of alertness that is very high so they can participate and swallow. Or are they unable to do that in the situation you're looking at? That means looking at the duration of the person's typical seizure.

Dr. Nathan Fountain:

[25:53](#) If you typically have seizures that last just a minute or less, then there's no rescue therapy that's going to kick in and work in one minute to stop that seizure. But if you have them in clusters over the course of a few minutes, then you'd have a medication you can take and swallow, let's say to prevent the next one, probably unlikely it's going to be a swallow medication. You can participate in taking the medicine by whatever form depending with the next one.

Dr. Nathan Fountain:

[26:16](#) On the other hand, if the typical seizure is five minutes and occasionally they're 20 minutes, then you need to have something you can give that is going to act quickly and which the person can't participate, whether it's rectal or nasal or intramuscular. So, let's think about the ideal rescue medication because that's really the... What we're after is an ideal rescue medication.

Dr. Nathan Fountain: [26:39](#) The ideal one is non-oral, meaning you don't have to take it, so you don't have to participate in getting it. It's quick acting, so to work almost immediately. It's simple. That means you can carry it with you. It doesn't require lots of mechanisms to put together or anything like that. It can withstand heat and cold and keep it in your car or your pocket. It is not sedating. So, if they give it to someone, they wake up from the seizure they're right back to themselves, that would be ideal.

Dr. Nathan Fountain: [27:03](#) It can be used frequently because one problem with benzodiazepines is that it sometimes wear off. Because if these are such great medicines that stopping and preventing seizures, why not just take them every day? That's a perfectly logical question. Unfortunately, the answer is for most of these, if you took it every day to prevent the seizures, effects tend to wear off. If you're taking it every day and those effects wear off, and then you do have a seizure emergency, sometimes it's difficult to find a medicine like this to stop the seizure.

Dr. Nathan Fountain: [27:32](#) So, we don't tend to like to use medicines like this that has benzodiazepines for the ongoing treatment of seizures. We'd rather reserve them or save them for abortive therapy or rescue medications. Of course, there are some people that do need to take them every in specific situations and your epilepsy doctor, the epileptologist you see in that situation will work through that.

Dr. Nathan Fountain: [28:00](#) Let's talk about the details of these delivery methods. I've referred to lots of different things, and now let's get down to the nitty gritty. So, let's talk about the difference between oral medications and rectal medications. So, oral meaning taking by mouth, that would be pills or liquid. They're easy to administer. They're easy to store. They're easy to obtain. Pharmacy has a bottle of it on the shelf typically if they're pills. But you must be alert enough and able to swallow. The problem is it takes time to swallow it, so even that amount of time.

Dr. Nathan Fountain: [28:30](#) But then once you swallow it in your stomach, it has to break down. The medicine has to come out of the pill one way or another. It has to be absorbed into

your stomach and then into your blood. Then it has to get up to your brain. So, it has to get in your blood all the way up to your brain.

Dr. Nathan Fountain:

[28:43](#) Now, if you're not in a hurry, none of those matter. So under normal circumstances, when you're just taking a regular seizure medicine to keep away seizures doesn't matter if it's absorbed. All that stuff happens over minutes or hours, because you're just going to take the medicine one after the other, right? Say twice a day, for instance, or even once a day, it's going to stay in your blood. But in a seizure emergency, that matters because as we said, we're trying to stop the seizures quickly.

Dr. Nathan Fountain:

[29:08](#) Rectal medication has a definite faster onset of action than oral medication because as soon as it goes into the rectum, it's absorbed through the lining of the rectum. It's relatively simple that as you can direct people to simply put this in their bottom, there's a low likelihood of complications. So, one thing about being absorbed relatively slowly, so faster than the stomach, but slower than other methods, is that the peak drug levels don't peak as high. So, we'll talk about that in a moment with a specific illustration.

Dr. Nathan Fountain:

[29:36](#) But with levels, not as high, you're less likely to get complications from it. Also, makes it less sedating in some ways. But the problem is it's slow to administer. The reason it's slow is because you got to get all the apparatus out. You've got to take the person's pants down and so forth. It's absorbed relatively slowly compared to say intranasal, or intravascular certainly IV. It's uncomfortable. If you're awake, you don't want to participate, obviously. It's socially unacceptable.

Dr. Nathan Fountain:

[30:02](#) What I mean by unacceptable is that most people would not volunteer to do it in public. So, those are important things to consider. Now, let's talk about intramuscular and intranasal administration. So, intramuscular injections. That's a shot through a syringe with a needle on it, into the muscle, let's say into the shoulders, not a typical place, but into the leg, for instance. It has a fast onset of action or relatively fast.

Dr. Nathan Fountain:

[30:27](#) The problem is it's difficult to keep syringes and needles available. That's inherently complicated in our society. Storage can be complicated, so it doesn't necessarily have a long half life. And people have a lot of fear of needles. What I mean by that is people don't want to get injected with a needle. So, they have a certain fear of the acts, it's uncomfortable. Then people don't want to inject someone else with the needle. They fear that they're going to cause a complication, which is possible. It's surprisingly unlikely, but it's possible to cause that problem. So that's an appropriate fear, I guess you'd say.

Dr. Nathan Fountain:

[30:59](#) With intranasal administration of medication, just like, let's say, an Afrin nasal spray has blown up your nose, it has a fast onset of action. And for the reasons we talked about that medicine gets distributed up in the nasal passage is absorbed very quickly, it goes right into the blood and you administer it yourself. So, you're not reliant on anyone else. So, if you're awake and alert and able to participate, you can screw it up your nose yourself. It's portable, simply carry it in your pocket, for instance. It's discreet so that people can't necessarily see what you're doing compared to rectal, for instance. It's socially acceptable.

Dr. Nathan Fountain:

[31:32](#) So, everyone knows about putting medicines up your nose like Afrin. The problem is it requires normal nasal passages, which isn't usually a problem that can be. So at the very least, someone has to make sure you have normal nasal passages. It can be irritating. So, some of these things have taken surprisingly long to be developed because you might be saying to yourself right now, "Why didn't we do this 20 years ago? As soon as we thought of this, why didn't we do it?"

Dr. Nathan Fountain:

[31:57](#) The reason is because it's more complicated to think, it's more technology driven to develop intranasal medications. And so, that technology is relatively new. The reason is because you need a small volume as we mentioned. You have to be able to concentrate the medication more than normal. You have to have a mechanism that reliably squirts it up the nose and you have to do it in a formulation, so

the chemical itself, the compound is squirted up the nose, has to not be irritating. So for example, there've been, I guess, two developments of intranasal administration of medications that were delayed a long time because it causes irritation, the nasal pastures. It took a while to overcome them. So, it can't be irritating.

Dr. Nathan Fountain:

[32:41](#) If you're not using these sort of formulations I talked about if you're using the traditional IV formulation, let's say, which is a pretty big volume to squirt up the nose, then you're not really sure if it was delivered because it might just get squirted down the nose and be swallowed. Now we're back to the swallowing problem that takes a long time to be absorbed.

Dr. Nathan Fountain:

[33:00](#) So, let's be explicit about which rescue medications are approved for use. So, these are approved for use, but not necessarily approved for abortion or rescue therapies of seizures. Diazepam is approved for treatment of seizures, including Valium, the oral form. But until recently was the only FDA approved medicine to abort clusters in the form of Diastat, which is a rectal gel form of diazepam.

Dr. Nathan Fountain:

[33:32](#) Lorazepam, or Ativan is commonly used to stop seizures, but it's not really approved exactly for that use. It was developed a long time ago before anyone ever even thought of calling that something separate from treating a seizure. The same is true of clonazepam or Klonopin. It's not so often used as an abortive therapy to stop an ongoing seizure, but it's often used to prevent the next seizure in a cluster where it's long enough between the seizures. You can swallow a pill for instance, but it's not exactly approved for that use although it's used in that way.

Dr. Nathan Fountain:

[34:03](#) Midazolam in the form of IV, Versed, is not approved for treatment of abortive therapy or the regular treatment of seizures. But in the interim nasal form was just recently approved as a Nayzilam. So Nayzilam was approved end of last year, but it's still not available in pharmacies. This is intra Nayzilam Midazolam. I think it will be available in maybe by the end of the year, early part of next year, I suspect.

Dr. Nathan Fountain:

[34:34](#) Let's talk in detail now about diazepam in a pill form, which is commonly known as a brand name Valium, but is available as generic. In adults is typically given in 10 to 15 milligrams. The advantage is that it's familiar. 15 milligrams in an adult will definitely knock them out. So, if you take 15 milligrams pill for most adults, it will knock them out. Now for people with epilepsy who are taking other seizure medicines, particularly if you're already taking benzodiazepine medications of some kind, it may have less effect. This is where I hesitate to say 10 to 15 milligrams is typical in adults because everyone is different. So, talk to your doctor about that. It could be as low as five milligrams, it potentially could be more than 15 milligrams.

Dr. Nathan Fountain:

[35:20](#) Rectal Diastat. The rectal diazepam, we've been talking about, allows for a quick drug absorption as we said through the rectal mucosa. One important thing is that the dose has to be dialed on the syringe. So, if you look at the illustration over here, illustration three, this is from the package insert. So, this is from the actual instructions you'll get with the diazepam and you can see it has a dial on it. The dial has to determine how much is given.

Dr. Nathan Fountain:

[35:51](#) So be sure to ask the pharmacy to dial up the right dose. The advantage to this is that it's effective. It's inexpensive and generally covered by insurance. I guess inexpensive is a relative term, but it is relatively inexpensive. It's not FDA approved for stopping a seizure, although people commonly think of that. That's not really what it's approved for. But patients and also not surprisingly patients find delivery invasive and there are not very many adults that would volunteer to have a rectal medicine administered at the mall, let's say, out in public. So, this has really limited the use despite it being relatively effective.

Dr. Nathan Fountain:

[36:27](#) You can see in this cartoon over here on the right side of the screen, what's actually involved. So you have to prepare the syringe. So, that's one step. So first you have to have the syringe with you, then prepare the syringe, then take the person's pants down, make sure there's nothing obstructing their anus, and then deliver the medicine in their rectum, and then hold their cheeks together so it doesn't

come out and that's sometimes more competent than you think because it has to actually be absorbed, you're going to make sure it's absorbed to hold their cheeks together.

Dr. Nathan Fountain:

[37:00](#) So on the one hand, when this was developed and approved, it was kind of a godsend for some people because it would prevent the next seizure in a cluster, as it was used to grab the next seizure a cluster. Also, it's commonly used while someone is still seizing because there's possible to do but complicated and it's not exactly approved for that use.

Dr. Nathan Fountain:

[37:19](#) So on the one hand, it's great, particularly in people who can't participate while you're at home. On the other hand, it's kind of obviously a little bit invasive. So, let's talk about the difference between IV and rectal dosing of diazepam because this is really what we think about as physicians or in developing new drugs about how this works. Because remember, it's all about the time for the onset of action, how quickly it can work.

Dr. Nathan Fountain:

[37:45](#) At the other end, how long it lasts, how long does it continue to keep away the seizures? So, here in this graph, you can see that the circles is an IV doses... Well, first of all, let me explain the graphs. Over here is the blood concentration. Some up here is more and more concentrated in the blood, the level in the blood and over here is time and these are hours. So, if you look at the circles, as soon as you inject an IV medication, it goes way, way up because it gets all concentrated in your blood.

Dr. Nathan Fountain:

[38:11](#) It goes right in a syringe, in your vein, it's a whole bunch of your veins. Then it gradually comes down as it's distributed throughout your body, and then gradually comes out of your body. The triangles here is the rectal administration. So, you can see that it takes a little longer to kick in, but still kicks in pretty quickly. Now, the peak of this doesn't happen for about an hour, but you can see that achieves pretty high level. So, I can tell you as these levels go, it's a pretty high level after just a few minutes.

Dr. Nathan Fountain:

[38:36](#) So, my interpretation of this is that it takes about 15 minutes for the Diastat to reach a typical level, but it's progressively going up and up in the blood throughout that 15 minutes. So for some people, it'll achieve a good level to stop seizures in less than that. So, that's how we think about its onset of action. So, ideally, you want to have an onset of action in a peak level very quickly. Then you want to last a long time and that's this graph out here. So, you can see the levels still last a long time and last a bit longer with the rectal form in the triangles than with the IV form even.

Dr. Nathan Fountain:

[39:06](#) This usually is less of an issue because it lasts a relatively long time. So, how effective is it on randomized double-blind placebo controlled studies? So randomized means patients are randomly assigned to one treatment or the other. Double-blind means the physician doesn't know whether they're giving the drug or giving placebo. So that means just water in this case. This was compared against, and it's placebo controlled, meaning half the people get or a portion of the people get the drug and another portion get water essentially.

Dr. Nathan Fountain:

[39:38](#) What's called study one, we can look at the percent of the seizure-free for 24 hours. That was the main outcome and kind of easy thing to understand. If you think about preventing the next seizure, which is what this was about 62% of people who got Diastat, didn't have a seizure the next 24 hours. Whereas if you got water, only 20% were seizure-free for 24 hours. That's a pretty big difference. Now, there's a couple of things to know, not everybody does it prevent the seizure in this case 62%. So that means about 38% still had a seizure next 24 hours.

Dr. Nathan Fountain:

[40:08](#) But if you got water instead, so if you didn't get Diastat, then 80% had a seizure in the next 24 hours. These were people who are known to have clusters of seizures. That's why they were in the study. In study two, it was somewhat similar, a little narrower difference. But if you look at seizure-free for 12 hours, 55% who got the drug were seizure-free compared to 34% who got placebo for water. So, it's a little narrower difference. This has to do with how the

studies were conducted, but also over what period of time.

Dr. Nathan Fountain:

[40:37](#) So, the idea is that's pretty effective if you look just here at study one. That's why this is really what launched the notion that rescue therapies were effective and safe. So, lorazepam is only available in the pill form for outpatient use. It's familiar doctors kind of use it as their favorite form. The pill form has a longer onset of action. So, it takes longer to kick in than say, diazepam and Diastat, but we think it may last longer. There's not a lot of evidence for that. That's kind of the notion. It's not designed to go under the tongue as we said, but some people use it that way anyway. But mostly when you do that, it's probably mostly swallowed. It's kind of favorite in preventing the next seizure when it's likely to occur relatively soon and if you can give it IV.

Dr. Nathan Fountain:

[41:23](#) So doctors historically have preferred lorazepam, maybe that's changing, but that was true. That was true as an inpatient in IV form, but also it's probably true for giving people pills in the clinic. Clonazepam is only available on pill form in the United States. It's also familiar and has a long onset of action that may last a long time, which is why we'd like to give it rather than other things if you have to give a benzodiazepine every day to prevent seizures. As kind of a favorite in that way, that many doctors would rather give clonazepam if you have to take it regularly every day to keep away a seizure. But it takes a long time to kick in.

Dr. Nathan Fountain:

[41:59](#) So if the next year is going to happen a few minutes, that's not really going to help. Midazolam is really the focus of our discussion, I think. It's not available as a pill. It's great for short term treatment of seizure clusters or acute repetitive seizures. So, this is something that has a potential to both stop the ongoing seizure and prevent the next seizure, and maybe even to prevent a seizure from progressing.

Dr. Nathan Fountain:

[42:25](#) The intranasal form is approved as the drug Nayzilam, pretty clever name in May of 2019. But as I mentioned, it's not available in pharmacies yet. It allows for quick drug absorption because as the drug gets dispersed up the nose, it's then absorbed quickly.

It's indicated for people 12 years old and older for acute treatment of seizures. Its advantages, it has rapid onset of action, it's simple to use, and it's portable. So, here's the mechanism over here. It's very slick little mechanism.

Dr. Nathan Fountain:

[42:56](#) It has this plunger down here, something to hold onto, and this thing that goes up the nose and when you do, you can only depress it, probably it can't be depressed part way. So as soon as you start to depress it, boom, it'll depress all the way and deliver the whole dose. It's administered just like in this picture, which is pretty simple. There is a little bit of irritation with it sometimes. The incidents of this is relatively low actually. The uncertainty of delivery is only if you don't have an open nasal passage, so you don't have to breathe, you don't have to do anything because of the way that it's atomized in a very small volume that goes up the dose.

Dr. Nathan Fountain:

[43:32](#) If your nasal passages are normal, there's not much uncertainty in delivery. So, how effective is it? Well, in a pivotal study, 80% of patients who've got the drug, had their seizure terminated in 10 minutes. Now, and those who got placebo, they just got water up their nose or saline actually. 70% were stopped within 10 minutes. You'd say, "Well, that's not a big difference." But remember, these are studies of people who are having ongoing seizures. So, you don't know if their seizure is naturally going to stop soon, or if you're going to stop it soon with the drug. So, you'd expect that most of these people would have a seizure that did stop within 10 minutes. But what you're doing is trying to treat those people in whom it might go on longer.

Dr. Nathan Fountain:

[44:13](#) If you look at the preventive part of it, so for the next six hours, 58% of those who've got drug didn't have a seizure within six hours compared to 37% of those who got saline or placebo. So, this is pretty effective. It's not 100%. We'd really want something that stops things 100 percent of the time, and this didn't do that in these studies. Now, if you look at over the course of 24 hours, there's really no difference about whether you got a dose of midazolam or you got placebo, and that's not surprising because midazolam has a short half-life. You just administer

one dose. We expect you to work for the next few hours. We don't typically expect to work for 24 hours. So, that means the strategy here for all of these drugs is to give the abortive therapy then to do something to prevent the seizure in the longterm.

Dr. Nathan Fountain:

[44:58](#) What do you do to stop the seizure tomorrow? Because you've had a long one today and you might have a long one tomorrow. If you had a cluster today, you might have a cluster tomorrow. So with each one of these, you should be thinking about what are you going to do? Sometimes it's not doing anything, but sometimes it's make a change in the other medicines, the other seizure medicines you're taking, to grant the next seizure. It can cause sleepiness, which happens about twice as often you could take the midazolam and placebo. It doesn't happen frequently though. It can have some nasal discomfort, but with a single dose in clinical trials, there's no difference for a single dose, whether you got saline or you got the drug.

Dr. Nathan Fountain:

[45:35](#) So for a single dose up one nostril in the clinical trial, there was no irritability. It wasn't increased about baseline. But if you've got two doses, one up one nostril, and one up the other nostril, then in that case, those people have an increased incidence of nasal irritability. As I mentioned, physicians are really concerned that midazolam and drugs like that will alter breathing, will slow people's breathing or stop it. But there is no incidence of that in the clinical trial. For the kind of doses we're giving here is not really a problem.

Dr. Nathan Fountain:

[46:08](#) So how is this used? So, if we think again about the device here, each one of these devices contains five milligrams of midazolam and the idea is at the onset of a seizure or the onset of a cluster to deliver it up one nostril.

Dr. Nathan Fountain:

[46:28](#) If that works, great. If it doesn't work, then 10 minutes later, an adult could deliver a second dose of this up the other nostril. Typically, we'd suggest if you need more than that, my view if you need more than that, you need to go to the emergency room. Something else is going on. Or call the rescue squad if it's that urgent. It can't be given every day, so how

often can you give it? The instructions are and common clinical practice would be no more than a couple of times a week. So typically, we'd say no more than twice a week. If you got up to twice a week, we'd say you need to do something else to prevent the seizures from starting to begin with.

Dr. Nathan Fountain:

[47:08](#) Now, let's talk about the other things in development. What are under review by the FDA or in development? There's intranasal diazepam, which will be called Valtoco. That's already had an NDA or New Drug Application filed with the FDA. That means they'd completed enough of the studies that the sponsor thinks that the FDA should approve it and they sent that off to the FDA. What does that will be successful or not? Well, kind of what the FDA says and so forth.

Dr. Nathan Fountain:

[47:34](#) There's buccal diazepam film. What buccal means is inside the lip onto the gums, and you can kind of think of it like under the tongue, but instead of under the tongue, it can just be on the side of the mouth. That'll be called Libervant, I believe. Then there's also inhaled alprazolam, which will be called Staccato.

Dr. Nathan Fountain:

[47:54](#) The intranasal diazepam has published preliminary results of open-label pharmacokinetic in longterm safety studies. What that means is that because diazepam in the rectal form is already approved for use to treat seizure clusters, the main purpose or strategy in developing this is to see that the intranasal form is absorbed and has the same blood levels as the rectal form. So, those studies have been completed. There are longer term safety studies, so that means giving the drug to more and more people to see it's going to be safe and there's no unanticipated or unexpected problems. Those are ongoing or finalizing.

Dr. Nathan Fountain:

[48:38](#) Buccal diazepam is illustrated in this picture here from the company's website. You can see this little film here. There are some breath mint films are kind of similar. You can imagine you put it under the tongue, you can put it on the gum here or in the cheap. Open-label pharmacokinetic studies have been completed. That means that studies were done

to see that if you use this per diazepam, it's absorbed similar to the rectal form because that's what would be the gold standard here.

Dr. Nathan Fountain:

[49:08](#) There's a single dose crossover with rectal gel that has preliminary results. That means half the patients got the rectal gel and half the patients got the buccal diazepam film. It looks like in the preliminary results that it has the same absorption and levels as the rectal gel, which is what you're really after to see that they're equivalent. So, the preliminary results look like that.

Dr. Nathan Fountain:

[49:28](#) But really we're awaiting the final analysis of the onset of action. So, how long it took in the comparison to rectal diazepam, did it work the same? Did it act the same? Did it stop seizures or stop the cluster to the same degree that rectal diazepam or Diastat did? So, that's awaiting a final review. Then inhaled alprazolam. Inhaled alprazolam should have very fast onset of action because when you inhale a drug and it goes into your lungs, it has a need access to the blood. The problem with alprazolam, it doesn't have a very long half-life. So, it doesn't stay in the blood very long.

Dr. Nathan Fountain:

[50:06](#) Preliminary studies have been done. So, there's a proof of principle study, meaning a study in which it's not designed to find a statistical advantage, just a study done to see that it seems like it probably ought to work. Five patients were given the inhaled alprazolam, and it seems to eliminate or reduce the EEG discharge in those photosensitive seizures. What I mean by that is there are some people with epilepsy and whom when your flashlights in their eyes, it causes a discharge on the EEG and the inhaled alprazolam suppresses that discharge on the EEGs. They don't have them anymore, and we think that's going to be a good surrogate marker. That is a substitute marker for controlling seizures.

Dr. Nathan Fountain:

[50:46](#) There's an ongoing effectiveness study, that's a double-blind placebo controlled study. So, some get the drugs, some get placebo. The idea is to see, did it stop the seizure within two minutes? So, this is a little different than the other studies we've talked about. The other studies we've talked about were designed

mostly at preventing the next seizure. So, these are designed at stopping the current seizure within two minutes or preventing the next seizure. So, that's a little different, obviously you have to be able to participate to inhale the device that's illustrated up here.

Dr. Nathan Fountain:

[51:18](#) So, we really reviewed a lot of things, maybe kind of a whirlwind review, I'm afraid, of rescue medications and the take home messages here are that everyone should have a seizure action plan. I hope that's implicit in what I've said, that if there's any risk of a prolonged seizure or seizure clusters of any kind, you should talk with your doctor about whether or not a rescue medication is useful. The current rescue medications we have are a little bit cumbersome one way or another, but we think inhaled or intranasal drugs, particularly the intranasal midazolam that was just approved, will be a lot less cumbersome and easier to use, and when they are, then hopefully this will have a wider use.

Dr. Nathan Fountain:

[51:58](#) Thank you.

Laura Lubbers: [51:59](#)

Great. Well, thank you, Dr. Fountain, that was a terrific review of the available and upcoming rescue medications or abortive therapies. I know we've got a little bit of time left for some questions, and I know questions have come in from our audience. So again, if you do have additional questions, please submit them into the Q&A tab, located at the bottom of your Zoom panel and click send and Brandon will start reading them aloud. I do think that if we run out of time to address the questions, we'll try to get answers back to you via email. So, Brandon...

Brandon Laughlin: [52:35](#)

Absolutely. I'll try to rapid fire off some questions here. However, actually many of the questions did get answered already, so that's great. One question that came in, Dr. Fountain, was, is there any reason not to use Diastat before a seizure in a child who has been seizing for five minutes? And if so, how long should you wait?

Dr. Nathan Fountain:

[53:02](#) There's exceptions to every single rule, but as a general principle of someone in it, if you've been prescribed rectal diazepam gel to stop seizures, and

you have, let's say, a child who's been seizing for five minutes, there'd be few situations where you wouldn't give them the rectal diazepam gel. There are times when you would think about that. So, there's a safety concern, and there's a treatment concern.

Dr. Nathan Fountain:

[53:28](#) So, the safety concern is if they've already gotten lots of other medications, let's imagine that you've already given them other benzodiazepines, let's say clonazepam or lorazepam, or even diazepam in a pill form an hour ago. And so, it's already in their blood.

Dr. Nathan Fountain:

[53:43](#) You might be hesitant to give them more without any kind of supervision. Or the second situation is if it's someone who's tenuous that might have a medical reason not to. But as a general principle, we give rescue medications and tell them, "If you actually time a seizure, five minutes is a really long time." We do this in the epilepsy monitoring unit. We admit people to the hospital, observe their seizures to figure out where they're from and so forth.

Dr. Nathan Fountain:

[54:08](#) So a common exercise is to ask people when we watched the seizure on the video, go by say, "How long was that?" And they almost always say, "Oh, that was five minutes." But you know what? It's almost always under 90 seconds a minute and a half. So while you're watching someone seize five minutes, it's kind of forever, especially the big convulsive seizure. So for convulsive seizures or medically serious seizures, you might say, usually we would advise giving the medicine after five minutes of seizure activity.

Dr. Nathan Fountain:

[54:36](#) Now, if it's a non convulsive seizure, or if you're not sure it's a seizure, that's a different situation. So, I suppose we could imagine a situation where you wouldn't give them medicine. It was in five minutes because it's a non-convulsive seizure and you think it's not causing any harm. Let's say it's just a staring seizure, an absence seizure. You're unusual to have one for more than five minutes, but there are specific situations when you might. Or if you're not sure that it's a seizure, so if you haven't figured that out yet, then maybe it would be okay to not give the medicine if it's something, as in, convulsive activity.

Brandon Laughlin: [55:08](#)

Great. Thank you. Another popular question that came through is, are there any reasons to administer rescue medications to individuals that may have one seizure without a cluster, that being a tonic clonic or a grand mal seizure?

Dr. Nathan Fountain:

[55:29](#) That goes back to really defining what it means to have a cluster. So as a casual observation, we can easily make the statement, "Sure. Give the medicine to prevent the next seizure." But if you think about this in detail as the FDA does, when they think about exactly what the medicine is used for, this starts with a careful history to determine what is a typical seizure for that individual.

Dr. Nathan Fountain:

[55:50](#) So if that individual has big convulsive grand mal or generalized tonic clonic seizures that typically lasts three minutes, but let's say they have three times in one day or even twice in one day and you want to prevent the next seizure, usually you'd let that seizure complete itself because it would almost take three minutes just to administer whatever you're going to administer.

Dr. Nathan Fountain:

[56:16](#) Typically, we'd let that seizure complete itself, then give whatever medicine is appropriate to prevent the next seizure. So, there are lots of situations. I'm glad that question was asked because in general, we wouldn't treat an acute seizure unless it lasted more longer than usual or more than five minutes.

Dr. Nathan Fountain:

[56:35](#) Now, as I said, five minutes is a long time. So by three minutes, everybody's getting all excited and getting ready to do something, call the rescue squad or given a board of therapy or do something because it will kind of take your five minutes to figure all that out. But for most people with epilepsy, they don't have a seizure that lasts longer than three minutes. In fact, if you measure it, it's usually less than 90 seconds and a half. Now afterwards, they may be zonked seemingly dead to the world for a long time, even half an hour sometimes.

Dr. Nathan Fountain:

[56:59](#) But the actual seizure part is typically less than three minutes and almost always less than five minutes. So, if you define the typical seizures, less than

five minutes, we typically wouldn't recommend the currently available abortive therapies. Maybe that'll change. Maybe if it turns out intranasal medications really worked very quickly and are very effective and maybe we'll get for ongoing seizures, but at the moment we would say no.

Brandon Laughlin: [57:22](#)

Great. Thank you. We do have time for one more quick question. Then like Laura said, we will try to do our best to get to those questions that have been coming in recently. Do you have any suggestions for rescue therapies in children younger than two, obviously because the FDA approved cutoff for Diastat is two years old.

Dr. Nathan Fountain:

[57:47](#) Yeah. That's a situation where you really need to talk to your doctor about that. There are other alternatives, everyone gets nervous in treating young children. I treat mostly adults, but because of the situation I trained, I see both children and adults. When they're less than two, it gets a little complicated because the dosing changes as well as the method of administration.

Dr. Nathan Fountain:

[58:09](#) So, I'd say talk to your doctor about that. For a prolonged seizure in those less than two, we have the same concerns that we have in those older than two. So, although the medications are only approved down to a certain age, in a particular situation, doctors can use them in those situations. So for example, the IV form of midazolam is definitely not approved to be blown up the nose until now. Still the IV form is not, but yet we would use that in certain situations when we knew the details warranted it. So being less than two, you could still use rectal Diastat for instance, or could use some other form.

Dr. Nathan Fountain:

[58:48](#) So, talk to your doctor about that and what might be best in that particular situation.

Brandon Laughlin: [58:52](#)

Great. Well, thank you again, Dr. Fountain, I'm going to turn it back over to Laura now.

Laura Lubbers: [58:57](#)

Great. Yes. I want to thank you as well, Dr. Fountain, that was again a terrific overview. This is an area where we need a lot of education to help understand the different options that are becoming

available for us as a community, so I really want to thank you again for sharing your expertise in this. I also-

Dr. Nathan Fountain:

[59:14](#) Thank you for having me.

Laura Lubbers:

[59:15](#)

Absolutely. I also want to thank the BAND Foundation for sponsoring this webinar, as well as all of our webinars this year. And I'd like to thank our audience for your time and attention, your interest in learning about this topic, and for your excellent questions. If you have additional questions about this topic or wish to learn about any other of CURE's research programs, please visit our website at [www.cureepilepsy.org](http://www.cureepilepsy.org).

Laura Lubbers:

[59:42](#)

I also want to mention that this webinar, as well as all of our past webinars and our future webinars, are recorded and available on our website and you can find them in the program section of the CURE website. So with that, I want to thank you, and I hope you all enjoy your day.