A CALL TO ACTION: MEFLOQUINE

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[BEGIN FILE]

DANIEL SULLIVAN:

Hi, this is Dan Sullivan again with the Sergeant Sullivan Center podcast, A Call To Action. And I want to tell you about one of our upcoming episodes which is going to focus on questions that you want answered. Which is to say, if there is subject matter related to toxic wounds, environmental war injuries, occupational injuries associated with military service, the health care related to these or disability claims related to these, if there is a question you want answered or an issue you want addressed, whether it has to do with burn pits or mefloquine or any kind of vaccine that may have caused – or an insecticide that may have caused an environmental illness, an occupational illness, if you want to hear information about the science and about what research is going on in the independent or the public sector, we want you to reach out to us and let us know what you want to hear a call – what subject matters you'd like to see A Call To Action focus on in the future. The way you can get ahold of us is to go to our website, www.sgtsullivancenter.org, sgtsullivancenter.org. Look for instructions on how to submit a prompt. Or you can give us a call at 202-261-6562. Or send us an email at info@sgtsullivancenter.org.

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DANIEL SULLIVAN:

This is Dan Sullivan with the Sergeant Sullivan Center podcast. Thank you for joining us and welcome. Today we have a very special guest, Dr. Remington Nevin and we're going to be speaking about the neurotoxic effects of a drug that was provided to and has been provided to many service members to prevent malaria. That drug is known as mefloquine. We're going to do things a little bit differently this time. We're going to be addressing this subject in three segments or three acts. And in the first act, we're going to talk about the history of this drug, its development and its use in the military. In the second act, we're going to talk about the era of its widespread use and problems that began to crop up associated with its use. And then the decline of its use in the military and reasons for that decline. And then finally in the third act, we're going to talk about the FDA coming to the conclusion to put a box warning on the chronic effects of the usage of this drug including a discussion of some chronic symptoms caused by it. We're also going to talk about the implications for veterans of – who are filing disability claims related to various diagnoses that may be related to the use of this drug. And then finally we're going to talk more broadly about the implications for the improvement of the delivery of care to service members and veterans who have been exposed to this and other neurotoxins that may be affecting their health after deployment or after military service. So that's what our plan is for today. Thank you so much for being part of this podcast by listening to it, for your support of the Sergeant Sullivan Center and its programs, and for your commitment to improved post-deployment health for those who are suffering from health impacts of toxic war wounds. Dr. Remington Nevin, thank you for joining us today here in our studio.

REMINGTON NEVIN:

Yeah, thanks so much, Dan. It's great to be here.

DANIEL SULLIVAN:

Excellent. So why don't we start by – could you tell us a little bit about yourself, your training and your interest – how your interest in this particular drug developed?

REMINGTON NEVIN:

Sure. I'm a former army preventive medicine physician. I attended the Uniformed Services University — the "West Point" medical school — and had a career in preventative medicine. And during my career, I was deployed to Afghanistan where I became very familiar with the military's use of this drug, mefloquine. And that's really when my interest in this topic began.

DANIEL SULLIVAN:

Excellent. So this drug mefloquine is an anti-malarial drug. What is malaria?

REMINGTON NEVIN:

Well, malaria is a very serious disease and military forces have had to contend with the risk posed by malaria for centuries. The US military developed mefloquine because of concerns of resistant malaria during the Vietnam War. We had been using another drug chloroquine together with primaquine and there was evidence that this combination was losing its effectiveness, and thousands of service members were returning home ill from malaria. It was almost threatening the war effort — it was such a serious problem. And this led to the very large-scale effort to develop mefloquine, beginning in the 1960s.

DANIEL SULLIVAN:

And what were the – what were they trying to create when developing mefloquine? What specifically were the hopes that would be achieved by this particular drug?

REMINGTON NEVIN:

Right. So mefloquine is just the latest in a series of related drugs that the military or the US government has investigated and developed, dating back to the World War II era. Of course in World War II, we were fighting heavily in the South Pacific and malaria was a very real threat there. But unfortunately, the enemy had quarantined all of our sources of what was at the time the most effective anti-malarial drug — quinine. And so we were forced as a government and as a military to seek alternative drugs to keep our fighting forces safe from malaria. The drug we used during World War II was called atabrine — also called quinacrine. The British called it mepacrine — and this was very widely used in World War II. But it had many disadvantages. It was known to be toxic. It would dye the skin yellow. Soldiers didn't like taking it. And of course in rare cases, it caused very serious psychotic reactions. And information about this very serious reaction was kept relatively quiet during World War II, as you can imagine, out of concern that the soldiers that knew of the side effect would stop taking it.

DANIEL SULLIVAN:

That's interesting. What is it about – before we get into discussing specifically mefloquine and its toxicity, what is it, to your mind, about anti-malarial drugs that would have an effect, a psychiatric effect or generate toxicity? Is there something unique about these drugs that cross the blood-brain barrier and cause some sort of neurotoxic reaction?

REMINGTON NEVIN:

Yeah, it's a very good question. How is it that a drug that's designed to kill the malaria parasite, how is it possible that these drugs have psychoactive or even neurotoxic effects? The class of drug I'm speaking of, the quinolines, of which atabrine can be thought a member — of which chloroquine and primaquine can be thought a member — and the most recent drug, mefloquine can be thought a member — these drugs all have at their core this chemical structure that permits it to pass through the membranes of cells, penetrate the blood-brain barrier, and it’s this property that allows the drug to be effective in battling the malaria parasite. The malaria parasite, you can think has a structure that somewhat resembles the blood-brain barrier in that the substances have to be able to cross it and accumulate within this structure in order to kill the parasite — and so it might be an inherent risk of anti-malarial drugs of this class that what make them effective as anti-malarials also pose a risk of psychotropic effects and neurotoxicity.

DANIEL SULLIVAN:

That is very interesting. So this particular class of drugs, since World War II at the very least, we have — by we, I guess, I mean we, the scientific community — those administering the drugs, the country — we have known that this particular class of drugs has neurotoxic effects.

REMINGTON NEVIN:

Oh, yes. And in fact that very word was used to describe this class of drugs as early as the 1940s. The inherent neurotoxicity of the quinoline class of anti-malarials has been well established for well over seventy years. But what makes this issue a little bit more complicated is that not everyone who takes these drugs will have obvious clinically significant effects. The most serious reactions that we see are what we call idiosyncratic. They seem to affect some

people and not others. And this can be very dangerous because they'll be experience developed within organizations and within the medical community that the drug is generally safe — and when people aren't familiar with the most extreme side effects — but particularly if these side effects are psychiatric — they're all that much easier to dismiss as anecdotal.

DANIEL SULLIVAN:

What is the current thinking in the medical community about how to talk to patients, in this case we're talking about patients of a particular occupation where the medication is being used preventatively, but how to talk to patients both in an occupational setting and in a civilian setting about the health effects like this that are idiosyncratic? What are the – what is the current thinking about how patients should be educated about these potential idiosyncratic health effects of such drugs?

REMINGTON NEVIN:

Yeah, that's a very good question, Dan. I still think there's a lot of confusion and misinformation within the medical community. It's still often thought by many that only those that have pre-existing psychiatric disorders or that have a pre-existing neurological problem are susceptible to these idiosyncratic effects. And that's simply not true. There's very little evidence in support of that hypothesis. These drugs are inherently neurotoxic. But only some people seem to suffer the worst effects. And we've known about this ever since, in the case of mefloquine, it was licensed in 1989. The product insert very clearly said that if you take this drug for prevention of malaria at a dosage of one tablet weekly, if you develop signs of anxiety, depression, restlessness or confusion, these could be considered prodromal — or an early warning sign — of what they described as, quote, "a more serious event" — whatever that means. And what this tells us is that these early symptoms which today we now recognize include things even as seemingly benign as vivid dreams or nightmares are an early warning sign that you may be susceptible to the more serious toxic effect of these drugs and in that case you must immediately discontinue the medication.

DANIEL SULLIVAN:

Do you know, were military personnel provided this insert when the drug was administered to them?

REMINGTON NEVIN:

No. In almost all cases, military service members were not provided with the warnings that the drug insert directed. And in many cases, military leaders and official policy documents served to undermine the FDA directed warnings. As late as 2009 — many years after the neurotoxicity of mefloquine was established — and many years after warnings in the media and congressional concerns were raised about the toxicity of this drug — a military policy document stated erroneously that psychiatric symptoms from mefloquine occurred at rates of only one in 2,000 to one in 13,000 persons — and this is off by at least a factor of a hundred. It was known in 2002 that when taking mefloquine at a dose of once a week, symptoms of anxiety and depression developed in between 1 to 10 percent of users. And these symptoms, if they develop, are an indication to immediately discontinue the medication. Our experience has been that most soldiers weren't informed of this and if they did experience these early prodromal symptoms, they were not given an opportunity to discontinue the medication and switch to a safer alternative.

DANIEL SULLIVAN:

Can you speculate as to — if you are inclined to speculate or do you have information that would point to why that wouldn't have been, that information would not have been provided to them?

REMINGTON NEVIN:

It's probably the same concern that led the military to restrict the dissemination or the discussion of information about the association of psychosis with atabrine use in World War II. Any mention that atabrine could cause psychosis could land one in serious trouble in World War II. That was an official military secret. And I suspect that that same level of concern — an attempt towards censorship of this information — led to the military either intentionally or unintentionally understating these important warnings in the product insert. The real irony, Dan — the real tragedy — is that had we been more upfront about the meaning of these prodromal symptoms — had we said this drug is seemingly well tolerated by many, but some of you — and not an insignificant number of you — will experience these prodromal symptoms, for those of you that experience them, please stop the drug, we'll switch you to another drug, for example, doxycycline — but for those of you that don't have nightmares, don't have anxiety, don't have depression, feel perfectly fine — you can continue taking the drug. And this advice, which was listed very clearly in the product insert ever since it was licensed in 1989, was never effectively communicated to service members. And had we done that, we may have been able to avoid many of the chronic problems that we're facing in our troops as a result of its toxicity.

DANIEL SULLIVAN:

And let's close this — the first act by talking, just if you could articulate for our listeners, what is the nature of this injury, this, as we now know, preventable injury, which in some cases could have been stopped had this warning been issued, what is the nature of this – I believe it's permanent brain injury for many people, is that right?

REMINGTON NEVIN:

So the FDA now acknowledges that certain neurological side effects from the use of mefloquine can in some cases be permanent. We don't have very good data from autopsy studies or many animal models to know exactly what's taking place with mefloquine. But looking at related drugs — closely related drugs that were developed and tested in the '40s and '50s — what we saw was that in certain animals, these drugs would cause widespread but very local microscopic injury to numerous centers in the brain stem and deep brain. So dizziness, for example, that's often a feature of mefloquine intoxication. It was often thought to be due to an effect of the drug on the inner ear. But we now suspect that this dizziness and the vertigo associated with mefloquine use actually represents brain stem injury. An injury to those centers of the brain stem that control input from the inner ear and that control, output control in the eyes and what not. So it's very difficult to diagnose. Oftentimes the effects can seem "aphysiologic" and challenge even the most skilled physicians. But microscopic and multifocal brain and brain stem injury is certainly plausible based on results from closely related drugs. And, Dan, the other effect is of course a broader post-encephalopathy syndrome. Even if the drug doesn't cause focal or microscopic injury, there's good reason to think that a broader, more diffuse, and chronic brain dysfunction can result from the toxic encephalopathy that acute poisoning with mefloquine can cause.

DANIEL SULLIVAN:

So, closing out the first act of our podcast, just reflecting on what we've learned so far, we've learned that anti-malarial drugs have been known to have a neurotoxic effect since at least World War Two. And that this particular drug, mefloquine, has a neurotoxic effect that can – that research suggests can lead to, at least in some cases, a permanent injury to the brain or brain stem. I think what particularly is relevant to the Sergeant Sullivan Center and its mission is that there was an opportunity here to provide every service member who received this drug with a warning about its potential neurotoxic effects which would have given them the opportunity to stop use of the drug and therefore to prevent the injury to their brains. This opportunity, it appears, was not provided to many if not all of the people who received this drug. The Sergeant Sullivan Center would strongly recommend that the Department of Defense begin to change its strategies for providing warnings to service members about the potential long term and short term effects of any drugs being provided them. And that's something I want to – we'll visit a little bit later on in the podcast towards the end about what can we do together to encourage better best practices for occupational health in the military medical establishment. We're going to take a short break right now and then we'll come back to act two.

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ANNOUNCER:

Down the street and across the country, with compassion and care, the Sergeant Sullivan Center's dedicated volunteers and supporters are fighting the battle against the toxic wounds of war. We invite you to join us in our life saving mission by participating as a runner in Team Sergeant Sullivan Center. We'll be running at various marathons that support various charity fundraising issues. We are the only 501C charity to focus exclusively on the issue of toxic wounds. For research and advocacy. We're making a difference. But we can't do it without your help. By joining Team Sergeant Sullivan Center, you'll be directly engaging in the battle for [UNCLEAR] For more information, visit us at sgtsullivancenter.org. That's sgtsullivancenter.org.

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DANIEL SULLIVAN:

This is Dan Sullivan. Welcome back to the Sergeant Sullivan Center podcast. Today, we're talking about mefloquine with Dr. Remington Nevin, who is the nation's leading expert on mefloquine toxicity and quite possibly one of the world's leading experts on mefloquine toxicity. Dr. Nevin, how many people are familiar with mefloquine toxicity and working on this right now, would you say?

REMINGTON NEVIN:

I would say over the last decade there's really only been a handful of researchers that have taken on this subject. It's not a subject that endears you to funding agencies — the military hasn't had much money to support research in this area for obvious reasons. But I suspect the ranks are going to grow significantly in future years. It's very much like what the research environment looked like for PTSD and traumatic brain injury in the early 2000s. There were very few that were studying these topics and after the military acknowledged the number of troops that were suffering from these problems, hundreds of millions of dollars in research funding was devoted to improvements in this area. And even if just a small fraction of that would be devoted to this area, we could see many more researchers enter the field and much progress made.

DANIEL SULLIVAN:

And that's what I hope that this podcast will help spread awareness of this issue and in part help bring about that shift, because focusing on this type of war injury is very important and it's important to the mission of the Sergeant Sullivan Center as well. The subject that we're going to talk about in the act two here is about some of the issues you just brought up. The era of widespread use of mefloquine, the problems associated with its use, and we're also going to — I'd like us to touch a little bit on the struggles that doctors in the military health care establishment may have had during this era with providing care to patients suffering from apparent neurotoxicity associated with the use of mefloquine. So if we could talk a little bit, first, what was— what would you describe, Dr. Nevin, what— during what era was this drug used in a widespread way, how many people were affected by its use and when did problems start cropping up in your perspective associated with its use?

REMINGTON NEVIN:

Sure. Excellent question, Dan. I would say that the period of widespread use where exposure to this drug was very likely or probable during deployment to a malarious area really spans the ‘90s and 2000s with certain exceptions. If you deployed to a malarious area any time during the ‘90s or 2000s, there was a good chance that you were given mefloquine — you were probably issued mefloquine in little baggies or just pill by pill by a medic once a week. Very little likelihood early on that you have documentation of this in your medical records. But it's important to emphasize, Dan — I've heard reliable stories from veterans, in some cases with documentation to match — that this drug had been used operationally throughout much of the 1980s on an experimental basis and possibly even in the late 1970s. There was recently a claim adjudicated by the VA where a veteran attested that he was given mefloquine experimentally during the late 1970s prior to a mission. This was entirely plausible based on what we know about the military's development of this drug, which did see it used in humans around that time. But for the most part, the majority of those exposed would have been exposed beginning with the Somalia operation throughout the 1990s, during special missions, Cobra Gold training exercises in Southeast Asia, assignment to the Korean peninsula during the time that the drug was used, and of course most significantly in the last decade, the wars in Iraq and Afghanistan were for many years it was the drug of choice.

DANIEL SULLIVAN:

Why is it that – why has it been the drug of choice?

REMINGTON NEVIN:

That's a very good question, Dan. Because our experience now is that really this is the least well suited drug. Our experiences most recently in Liberia show that the daily medicines are much better tolerated, there's better compliance, service members simply prefer the daily medicines. And of course the side effects associated with mefloquine have made this worse. Mefloquine was desired by the military I think because its weekly administration could simplify what's called directly observed therapy. So instead of relying on the service member to take the pill on their own and answer yes to their first sergeant that they took it, you could have a formation once a week and a medic could walk down the formation and dispense one tablet at a time and document that everyone was taking the medication, this has certain advantages from a commander's perspective, I can certainly appreciate that. But again, our experiences most recently in Liberia show that you can deploy thousands to the most endemic malarious area and safely use daily medications. So I think much of the military's rationale for wanting a weekly drug, I think that logic has been disproven recently.

DANIEL SULLIVAN:

And if I recall correctly, with this particular drug, there's a – in terms of its efficacy, it doesn't become effective immediately. It becomes effective after a period of time, is that right?

REMINGTON NEVIN:

Yeah. That's really the remarkable thing about mefloquine. The product insert even clearly notes that steady state — steady state levels of the drug are in some cases not achieved until seven to ten weeks into dosing. For many years it's been common within my profession, preventive medicine or travel medicine, to recommend that travellers take three tablets all at once or one tablet every day for three days as a loading dose to try to overcome some of the slowness of this drug in building up to protective levels. But this is a very dangerous practice. It increases the risk of prodromal symptoms and more serious events that transpire afterwards. Certainly I don't think a responsible travel medicine practitioner would recommend the use of loading doses today in light of the black box warning, but for many years this was commonplace. The advantages of a daily dosed drug that quickly build to protective levels are that you can begin it a day or two before travel to a malarious area and this dosing schedule is much more consistent with the way our forces operate. We don't have seven to ten weeks advance notice before we deploy overseas on a combat operation. In some cases, we just have a few hours. And so the daily medicines that quickly build up I think have always been better suited and the advantage, the professed advantages of weekly dosed anti-malarials, I think, have been broadly overstated.

DANIEL SULLIVAN:

So for the anti-malarials that are daily dosed anti-malarials, is doxycycline one of those or is that a different type of drug?

REMINGTON NEVIN:

So doxycycline is an anti-malarial. It was licensed as an anti-malarial in the 1990s. For whatever reason, the military has never devoted as much interest to the tetracycline class of drugs as anti-malarials as it did towards the quinoline class. But before mefloquine was licensed in 1989, doxycycline, the antibiotic doxycycline was the military's drug of choice for prevention of malaria in areas where there's resistance to chloroquine. And of course, in recent years, as the military's gradually moved away from mefloquine, it first went back to doxycycline for widespread use in Afghanistan. And when it did, we saw a dramatic drop in the rate of malaria, which I believe is due to the improved compliance that soldiers have with daily doxycycline.

DANIEL SULLIVAN:

So daily doxycycline as an alternative to mefloquine actually showed — appeared to be more effective to prevent malaria? Is that – am I interpreting that right?

REMINGTON NEVIN:

Yeah. And that's a key term, effective. There are two terms in drugs — that is efficacy and effectiveness. And effectiveness is most important in this context because a drug, no matter how efficacious, will not work if it's not taken — or if it cannot be taken safely. And doxycycline, what we see is that soldiers tend to be more compliant with the dosing schedule and — of course, that makes sense, right — because a fair percentage of soldiers will need to discontinue mefloquine should they develop a prodromal symptom such as anxiety, depression — now we understand the dreams or nightmares. But of course, then, we're forgetting the third drug, a combination drug that was also developed by the military — atovaquone-proguanil, marketed as Malarone. For many years the military was reluctant to use Malarone because it cost about five to seven dollars a tablet. In contrast to mefloquine which was maybe five dollars a tablet per week and doxycycline, of course, was always just pennies a dose. But for many years, commanders and senior medical officers were reluctant to devote the money necessary to pay for large amounts of Malarone for deploying troops. But of course, this is a false economy. We now know it costs about a million dollars to deploy a service member overseas for a year. And the cost of even the most expensive drug, Malarone, is just a few thousand dollars in comparison. So it's a false economy to avoid use of that drug if it's best in that setting.

DANIEL SULLIVAN:

Do these other drugs, doxycycline or the other two you just mentioned, do they have any known neurotoxic effects? Or are they – would you, can you accurately describe them as safer in that regard than mefloquine?

REMINGTON NEVIN:

I would say doxycycline is certainly safer from the perspective of psychiatric and neurologic effects. Atovaquone-proguanil, there are troublesome signs that this may be similar to mefloquine. It's somewhat related chemically. In some sense, one of its components has a similar mechanism of action. And so there's reason to be cautious. But there's

certainly less reported problems with Malarone than there were with Lariam or mefloquine when it was first developed. But I do think with anti-malarials, because the nature of parasites and the similarities between some of the structures, that we need to be cautious and keep an open mind of the potential mental health effects from all classes of anti-malarials.

DANIEL SULLIVAN:

Let's talk a little bit about this – two things, I think, when did we start seeing problems during this era of widespread use, but actually, before we get into that, could you touch a little bit on the problems that were identified during the development of the drug and then the problems that we began to see when it was used in a widespread way?

REMINGTON NEVIN:

So we knew that this class of drug from our experiments in the ‘40s and ‘50s were associated with — let's say — two different main problems. The first was neurological illness or disease. Mostly dizziness, but sometimes parasthesias or tingling in the hands and feet. And visual disturbances. Occasionally chronic intestinal problems. All of which we learned in the ‘40s and ‘50s could be best explained by neurotoxic injury to brainstem centers. Once you cause injury to various brainstem centers, almost every system in the body can be affected. But these drugs seemed to focus their worst effects on the vestibular systems, the visual system, sometimes the autonomic system. And sometimes the peripheral sensory system. So this was well known. And we saw clear evidence of this aspect of the drug's toxicity when it was first tested in the 1970s — clear evidence of all of these problems. The other syndrome that we knew about was associated with this class of drugs was the encephalopathy, what I call limbic encephalopathy. Or the dysfunction of those parts of the brain that control memory and emotion. We knew that atabrine could cause cognitive problems and even amnesia. It could also cause mania, paranoia, and psychosis. This was all very well established and numerous other quinoline drugs that were developed around that time show these same effects. And during mefloquine's development, we saw clear evidence of this prior to licensing with case reports of amnesia, confusion and psychosis.

DANIEL SULLIVAN:

Limbic encephalopathy, is that something that shows up on an MRI?

REMINGTON NEVIN:

No. And it's important to emphasize that there's really no reason to think that any of these effects would be visible on MRI. MRI is capable of revealing structural anomalies in the brain, but this is a microscopic injury. It's an injury to a specific type of neuron in a very small area of the brain. And so it's not the same kind of damage that occurs when you have a large trauma to a whole portion of the brain, it's not the same type of damage that occurs when you have a blood vessel blocked leading to stroke. The drug is exerting a chemical toxic effect, a neurotoxic effect only on certain types of cells in certain scattered areas of the brain. And so the only way I think to definitively diagnose this particular effect is autopsy. And of course this is not uncommon, right? Often the effects of traumatic brain injury will not be visible on imaging. We're learning about the effects of chronic traumatic encephalopathy and how that's able to be diagnosed at autopsy. Perhaps with technological developments, we'll find a way to image some of the worst cases of toxicity indirectly or remotely. But the technology is not there yet and in virtually all of the cases I'm familiar with, MRI and CAT scans are completely normal.

DANIEL SULLIVAN:

What would – so the symptoms of somebody who has this type of injury, what would they be like? How would you describe them?

REMINGTON NEVIN:

Well, there are two broad classes of symptom. And this is all described in the product insert. There are psychiatric symptoms that can begin with symptoms as mild as a personality change, a sense of unease or foreboding, vivid dreams, perhaps nightmares, disturbed sleep. But with time or increased dosing, these symptoms can build to paranoia, mania, in some cases depression. And psychosis can quickly take over. And of course the symptoms of psychosis can be delusions or hallucinations. In some cases, the individual is confused. And that's the primary symptom. They have difficulty remembering or they have difficulty concentrating. In some cases, they may experience a dramatic retrograde amnesia where they forget entire aspects of their past. Or it may be an anterograde amnesia where they're incapable of making new memories for the duration of the intoxication.

DANIEL SULLIVAN:

So during the era of widespread use, did patients, to your knowledge and personal experience, present with these symptoms? And did they receive care that was – that addressed the potential injury by the drug, by mefloquine?

REMINGTON NEVIN:

Right. Excellent question. And for the most part, the answer to that is no. And there are a few very well described cases of this. The most famous perhaps is that of Andrew Pogany. Staff Sergeant Pogany who deployed in the early years of the Iraq War. After a few tablets of mefloquine, he experienced a horrific hallucination and series of panic attacks. His nightmares bled into his waking moments and as he was asleep at his team house in Iraq, he awoke to a terrifying hallucination of his team house becoming under attack. He donned his combat gear and conducted a tactical room-to-room search. I mean, he was horrified. He was aware that he was hallucinating — seeing his teammates as mangled corpses. He was very much aware it was a hallucination. But he was powerless to stop it. He was powerless to stop the hallucinations from occurring. And when he, in desperation, asked his teammates for help, when he asked his medic for help, when he said he was losing his mind and he needed help, he was deemed a coward. He was deemed to be suffering from a combat stress reaction. And he was actually threatened with death had he been found guilty of cowardice. And many months elapsed before his initial diagnosis of combat related stress and ultimately post-traumatic stress disorder was reconsidered in light of new evidence that he had a comorbid vestibular disorder. So Andrew Pogany's case I think probably indicates that there many individuals that suffered some symptoms of mefloquine intoxication. Even things as mild as, seemingly as mild as anxiety or depressive symptoms that were misdiagnosed. In the context of deployment it's very easy to confuse the symptoms of mefloquine intoxication with those of combat stress. And in fact, it's virtually impossible to distinguish the two for certain. And for that reason, I question how we can have ever claimed to be using mefloquine safely. If the product insert says you must discontinue the drug at the onset of depression or anxiety, how is a commander to order this drug to be used safely in a combat zone where these symptoms are of course highly prevalent.

DANIEL SULLIVAN:

And what would happen if anyone raised that kind of concern to superior officers? The concern you just expressed, during the deployment setting?

REMINGTON NEVIN:

Right. So today, of course, the military accepts that these prodromal symptoms do occur. The military accepts that if a service member takes mefloquine on deployment and they develop any of these symptoms, they should be immediately switched to another medication. We use mefloquine on deployment now very, very rarely for those reasons. And the military I do believe now acknowledges that mefloquine can cause in some cases permanent disability. But in the 1990s and in the 2000s, before the black box warning, clinicians that suspected that it could be the drug that underlay some of these symptoms in a service member, I think in most cases they were discouraged from either documenting this, reporting it to the FDA, or pursuing this line of inquiry further. We know from media reports that one senior medical officer was encouraged to change his diagnosis when he stated that a group of service members returning from Iraq with vestibular problems, that these were due to the toxic effects of the mefloquine. And I believe psychiatrists and neurologists who were investigating similar associations with other symptoms were also in many cases either directly told not to document that or simply knew that pursuing that line of inquiry was not beneficial to their careers.

DANIEL SULLIVAN:

So we're going to now wrap up act two. And I just want to kind of cap what we've just discussed. We've talked about the era of widespread use of the drug mefloquine. The fact that the symptoms of mefloquine intoxication or neurotoxic injury associated with mefloquine can be indistinguishable from those of post-traumatic stress. And that many patients who exhibited erratic behavior or service members who may have exhibited erratic behavior or PTSD-like behavior during and after deployment may actually be suffering from a misdiagnosed or undiagnosed brain injury. I think what we talked about also points to the importance of providing information to medics and any military medical personnel providing care to to deployed personnel who received this drug, with information about its neurotoxic effects. We also addressed the pressure physicians and medical staff may have been under to, while providing care, that may have interfered with their ability to address the neurotoxic injuries of this particular drug. Which is now not used in as much of a widespread way – is it, before we close out, Dr. Nevin, is this drug still in use?

REMINGTON NEVIN:

Unfortunately, it still is. And I question why the military insists on keeping it on its formulary. In late 2013, US Army Special Operations Command, the command with probably the most experience with this medication very wisely

banned its use outright. They recognized its use safety simply was not possible in military settings. But the military insists, the broader military insists on keeping it on its formulary as, quote, “a drug of last resort”. And of course this use of mefloquine as a drug of last resort is not possible. It's not consistent with the product insert as the product insert guidance very clearly says that if you're taking mefloquine and you develop these prodromal symptoms then you must stop the drug and switch to another medication. But of course if mefloquine is your drug of last resort, then what other drug is there to switch to in the event that you develop prodromal symptoms? And we've seen thousands of prescriptions for mefloquine in the last few years. I question whether these individuals deploying to malarial areas would feel safe discontinuing the drug as the product insert directs should they, for example, develop anxiety or depression.

DANIEL SULLIVAN:

Well, hopefully this podcast will be part of the mission to educate patients and doctors about the neurotoxic effects of this drug even as it still remains in use as a drug of last resort as we begin to address some concerns that we have with the broader DOD, VA delivery of health care to service members and veterans with toxic war wounds. We're wrapping up act two right now and in act three we will discuss the FDA boxed warning of the chronic effects of mefloquine, implications for veterans who are filing disability claims related to this injury and some broader issues about the DOD and VA. Thanks for listening. We'll be back in a bit.

[MUSIC]

DAN SULLIVAN:

Hello, this is Dan Sullivan, executive director and one of the co-founders of the Sergeant Thomas Joseph Sullivan Center here today to talk to you about a very important project that we are initiating and a project that we need your help to make successful. And that is that the Sergeant Sullivan Center, its staff, its board of directors, and its board of advisors are beginning to work on an advocacy project to encourage a complete overhaul of the DOD and VA approach to treating environmental injuries and environmental injuries associated with military service. And the way we're going to do this is we're going to submit statements, a series of statements to independent agencies that provide advice to the Department of Defense and to the Department of Veterans Affairs. That would be the Institute of Medicine and the Defense Health Board. These eminent bodies are peopled by scientists that are independent, that have the ability to make independent recommendations to the Department of Defense and the Department of Veterans Affairs. They usually only hear from scientists that work for the DOD or work for the VA. They usually do not hear from the men and women who served in the armed forces. And they do not hear what each of you have gone through after suffering from an environmental injury during the course of your military service. And they don't hear about the deficiencies in the care that you've received. We want to change that. We believe that if the Institute of Medicine and the Defense Health Board hear from you, hear from the patients who are struggling with environmental injuries and from the health care providers who are seeking in the independent sector to get solutions for these problems that we can change the DOD and the VA approach to treating occupational and environmental injuries associated with military service. So what I need from you and what the Sergeant Sullivan Center needs from you is we need your story. We need to know about your environmental injury if you've sustained one and the struggles that you have faced in getting a diagnosis, in getting treatment, in getting the host of services that you should be provided for such an injury. Whether you sustained that injury in deployment or whether you sustained that injury over the course of your military service in another action related to military service. We want to know the struggles that you face so that we can share that with these eminent bodies. If you're a scientist or a researcher and you have a recommendation that you would like to make to the Department of Defense and the Department of Veterans Affairs about how to make things better, how to improve the delivery of care for environmental and occupational injuries, we want to hear your statement, too. We're collecting these statements and we're going to submit them to the Defense Health Board and the Institute of Medicine and we are going to ask for a complete overhaul of systems and an improvement of care for environmental injuries and the restoration of honour for toxic wounds. Together we can make a difference. If you have a statement you would like to submit, please submit it to info@sgtsullivancenter.org. That's sgtsullivancenter.org. Or just go to our website and you'll find instructions there on how to submit your statement. That's www.sgtsullivancenter.org. Thank you very much. [MUSIC]

DANIEL SULLIVAN:

This is Dan Sullivan with the Sergeant Sullivan Center podcast. We're now in our final act, act three, segment three. Talking about mefloquine toxicity and the neurotoxic effects of this drug as one of the toxic wounds of war. Speaking today with Dr. Remington Nevin, a mefloquine toxicity expert. Dr. Nevin, what we now — as we talked about in the last segment, and correct me if I misstate any of these things, mefloquine, while being once the drug of first resort to treat or prevent malaria, is now the drug of last resort. What do you think was the reason why mefloquine is no longer the drug of first resort and was there a particular instance that occurred that led to or you believe might have led to the military's decision to change its use of this drug?

REMINGTON NEVIN:

Yeah, that's a great question, Dan. It really is a stunning reversal. And the military's never fully explained why this drug which was introduced to much fanfare after investing hundreds of millions of dollars in its development, being labeled the drug of choice, has now been relegated to the back of the medicine cabinet, is now listed as the drug of last resort. Military officials emphasize it should be used very sparingly. The military's never explained why that remarkable change has taken place. I think, Dan, it's probably a number of things. Over the years, concerns with the drug accumulated. The manufacturer of the drug, Roche, stopped defending the drug as vigorously in the press — the advocates for use of the drug gradually were silenced. And so all that was left of course was the concerns of those who had been injured by the drugs and scientists such as myself advocating for greater controls and restrictions on its use. I think the tide began to turn in the late 2000s. When I was in Afghanistan, I was very surprised to discover that a sizeable percentage of those that I had deployed with had listed contraindications to the drug's use. And this means they deployed to Afghanistan with a diagnosis of depression or with a diagnosis of anxiety disorder and in some cases had deployed on antidepressants or anti-anxiety agents. And about one in ten service members, I did this study in 2007, had one of these conditions and were nonetheless deployed. And so of course under those conditions it makes it very difficult to use mefloquine safely because you're not supposed to give mefloquine to someone who's already anxious or depressed. My research went on to show that of those with contraindications, reasons not to take the drug, incredibly one in seven had been given the drug nonetheless. So they had been issued the drug contrary to military policy, contrary to the guidance written in the product insert, and of course not in keeping with good medical practice. Very risky practices and I think that the military in light of that research, upon confirming it independently, decided it should move away from mefloquine. But I think the initial decision to move away from mefloquine, and this happened first in 2009 with the Army and then later with the other services, I think that was made by military officials mostly out of concern with these contraindications. And it was only later that the military recognized that even those who are perfectly healthy and without contraindications when they deployed, they too can suffer problems. And so what we've seen is gradual strengthening in policy on restrictions in the drug's use. Culminating, of course, with the reemphasis after the black box warning that mefloquine should be a drug of last resort in the military.

DANIEL SULLIVAN:

So just going back to what you just said about – so there is a contraindication or it would not be military, the military has a policy against or did have a policy against prescribing mefloquine to people with pre-existing anxiety or depression?

REMINGTON NEVIN:

Oh, yes. And in fact since 2002, 2003, the product insert that's provided by the manufacturer has been very clear on this. That the drug cannot be used in individuals with mental health problems. But the reason for this, Dan, has been misunderstood over the years. It's often erroneously thought that only those individuals that have pre-existing psychiatric history are susceptible to the drug's toxicity and that's simply not true. The drug is a neurotoxicant and can cause this reaction idiosyncratically in just about anyone. And we don't know what the risk factor is. But it is not the same risk factor that causes mental illness. What happens, though, and the reason this contraindication exists is that the product insert of course says you must stop taking the drug if you develop symptoms of anxiety or depression. And what we see time and again is that individuals who have pre-existing depression or pre-existing anxiety, if those symptoms are under control or maybe in remission and they start mefloquine and they develop a new anxiety or a new depression as a result of the drug's toxicity, it's very easy for that patient and their provider to dismiss those symptoms as simply due to the existing condition. And so they'll continue taking the medicine. The product insert warns that if you don't stop, you could risk a more serious event. What could be more serious than anxiety, depression, restlessness or confusion? — of course: psychosis and permanent neurotoxicity resulting in neurologic disease. And so that's the reason we don't give the drug to those with contraindications — because it confounds or complicates recognition of a developing intoxication. Even individuals without those mental health histories can still be susceptible to this toxicity.

DANIEL SULLIVAN:

Let's talk about some of the potential severe reactions to this drug in terms of intoxication and acute responses. Is there any indication that this drug causes people to either become suicidal or violent?

REMINGTON NEVIN:

I think the association with suicide really should not be in question, Dan. And this follows from what we know about the basic epidemiology of suicide. Suicide has what are called distal and proximal risk factors. Proximal risk factors are the things you hear the military emphasizing all the time. Financial problems, stress, pain, intoxication with alcohol. But these proximal risk factors alone cannot result in suicide without the presence of a distal risk factor or an earlier risk factor. And what we know about the epidemiology of suicide is that the most common distal risk factor is pre-existing

psychiatric illness. Almost all suicides occurred in individuals with a mental health disorder. And because mefloquine can cause lasting mental illness and because mefloquine can trigger proximal risk factors, insomnia, heightened anxiety, it stands to reason that mefloquine can cause suicide. The causal association of mefloquine with suicide should not be in doubt if we accept mefloquine causes anxiety and can cause lasting mental disorders. It stands to reason from the known epidemiology of suicide.

DANIEL SULLIVAN:

You know, this raises kind of an interesting issue. I recall just recently speaking to someone who had been, who had a mefloquine injury essentially verified by physicians and he told me that he believed that he was going crazy before he received this diagnosis. And that he also believed that people who have been injured in this way and never learned that this was their injury might be led to commit suicide because they didn't think there was a way out, there was no way to explain what's happening to them. They didn't know what was happening to them so they felt lost. Is that something that you think is happening to people?

REMINGTON NEVIN:

Yeah, absolutely, Dan. You've really hit the nail on the head. You'll recall what I mentioned earlier happening Sergeant Pogany, that sense of utter horror at the changes they were experiencing, the hallucinations, the unreal sense for which no experience in life could prepare them. Feeling completely out of control. And desperately seeking an escape from this. It stands to reason that individuals suffering their own personal horror not understood by others, many times with no obvious external manifestations, will sometimes seek escape through suicide. I think there are a number of different mechanisms taking place that contribute to suicide. In some cases during acute intoxication, an individual may become psychotic and dissociate from reality. And in those cases, this can trigger the sort of impulsive horrific suicides we occasionally hear about when people will jump from a building very impulsively, will casually pick up a weapon and shoot themselves quite horrifically. Many soldiers know of events like this happening and wondering how – what could have driven someone to do this? If the suicide seems very odd and not in keeping with the individual's character and they were taking mefloquine, it's possible that an acute psychosis from mefloquine may have played a role. But what you mentioned I think is probably underlying more suicides. It's chronically – after one has recovered somewhat from a mefloquine intoxication, one's personality has changed, one might be forgetful or struggling with new impairments that others doubt, discount, might even accuse them of malingering, and this can be very depressing and cause many to lose hope and I do think that sort of despondency that comes with not having their condition diagnosed correctly or understood has led many to suicide over the years.

DANIEL SULLIVAN:

Yeah. And that's an issue of critical importance to us, to why we've founded the Sergeant Sullivan Center and our mission which is that we believe that similar to this fellow who told me about his own experience with mefloquine and his belief about it, we also believe that for every one of these toxic wounds, having an understanding of the diagnosis actually is a tool that can lead to greater health. But it can be hard to articulate to medical doctors, researchers, and scientists what that – how do you prove that scientifically? How do you prove that – because they sometimes, the argument that comes from the medical establishment is the opposite, that if you tell the patient what's wrong with them, it will make them sick. Or they will think that they're sick when they're really not. Or they'll manufacture symptoms. Whereas I think we believe the opposite which is if somebody is experiencing symptoms, giving them a framework for understanding those symptoms, even if it's an emerging framework actually gives them the tools that they need to improve. Is there any way that we can articulate that in a way that – in the language of science, or can you articulate that in the language of science?

REMINGTON NEVIN:

Excellent question. Good points, Dan. That's precisely the nature of my current research. We need to recognize that these lasting effects from mefloquine aren't side effects that should be thought of in isolation. But they're actually symptoms of a consistent syndrome of drug intoxication. What we're dealing with here is basically a new disease that hasn't been recognized as such for many decades. And it's primarily a psychiatric disease. Occasionally there are neurological manifestations, but the vast majority of those who are suffering to some degree from the toxic effects of mefloquine, they have what is for all intents and purposes a psychiatric disorder. And how do we diagnose psychiatric disorders? There is no scanner in which we can put someone, there is no blood test — all we have is questions and responses to those questions. So it was already well established that once a diagnosis is defined and diagnostic criteria are developed, that you simply ask the questions and you can determine the diagnosis. But we don't have those specific questions for this mefloquine syndrome just yet. That being said, the product insert lists those lasting symptoms that are associated with this disorder. Many individuals returning home from war that didn't experience significant combat stress or who didn't suffer a head injury but who nonetheless suffer with lasting cognitive problems, changes in mood, personality, sleep disorders to include abnormal dreaming or nightmare disorders, a sense of paranoia, anxiety,

depression, panic attacks, possibly a fear of crowds and then certain other symptoms that may be more physical to include visual sensitivity in certain settings, a sense of dizziness or unsteadiness, abnormal gait or vertigo, all of these symptoms together or a number of them in isolation could be consistent with the lasting toxic effects of mefloquine. And simply recognizing that this drug has these effects and can explain so many of these symptoms that didn't exist prior to deployment that developed when a service member comes home can provide that veteran with tremendous relief.

DANIEL SULLIVAN:

What do you think about actually telling – there's been an aversion within DOD to giving the product insert to service members. I guess for fear that they wouldn't take it. But I think what you've just said raises an interesting question which is if you did give the product insert to people then if – a certain number of people may, well, I think pretty clearly will enter into some kind of a psychotic episode as a result of this drug. So having the knowledge that that psychotic episode might originate from the drug, do you think that could potentially stop someone from acting out or to understand what's happening to them and seek medical attention rather than perhaps act out to the full logic of the psychotic episode?

REMINGTON NEVIN:

Yeah. Excellent point. So I recommend, when I'm advising clinicians who are considering prescribing this drug, I recommend that they provide very detailed instructions and guidance. Not only to the patient, but to their travelling companions. As to what some of the early prodromal symptoms of this intoxication might look like. We've seen time and again there are many cases where individuals on mefloquine have entered into a frank psychosis where they're actively hallucinating, where they're dissociating, and because they're not around their close relatives, they're in a military unit with individuals that may not know them very well, it's virtually impossible to detect in a military setting that individual is becoming psychotic. They may not be violent. They may be very quiet. And of course in military settings that can be advantageous. And so I think if one is to continue using this medication, and that's a very iffy proposition, but if one is to continue using this medication, there needs to be much greater awareness within the medical community, within those travelling with the individual, as to the subtle signs that one should be assessing that might indicate a developing toxicity. And of course, many individuals can recognize these themselves. If they wake up after taking mefloquine having had a very bad nightmare — the European drug insert now warns that you must immediately stop the drug — a nightmare or an abnormal dream is a reason to immediately stop the medication. Any anxiety, any depression, any restlessness which I take to mean disturbed sleep or insomnia, or confusion is of course reason to immediately stop the medication. But of course, the problem is if you know that you're confused, then you're probably not confused. And so there's just an inherent problem with the logic of the product insert. Expecting someone who is suffering intoxication from the drug to recognize their intoxication and act accordingly, it's almost as though the product insert is advising you to know when you've had too much to drink and decide not to drive home. If you are so intoxicated that you shouldn't be driving home, you're probably going to make the wrong decision and think you can drive home and the same problem applies with mefloquine. That by the time you're intoxicated enough, then you may no longer be able to act on the intoxication and discontinue the medication.

DANIEL SULLIVAN:

One of the things we planned on discussing in this third segment is the implications of what we've been talking about on veterans who may be suffering from disabilities related to this injury and filing claims. So we've now – we've discussed the injury, the neurotoxic injury associated with mefloquine and we've also touched on the FDA boxed warning. I wonder if you could articulate for our listeners how the science of mefloquine toxicity and the FDA warning about mefloquine toxicity may relate to claims that a veteran may file for health care and benefits related to this injury.

REMINGTON NEVIN:

Yeah. Excellent question. So the VA is very quietly, without making much of a big deal about this, they are very quietly now awarding claims for disorders that veterans believe are due to the effects of mefloquine and so there is a service connection being established for a number of diagnoses. I've seen a number of these claims come across my desk. The problem for the VA is as follows. The military has conceded – in fact, the highest ranking physician in the military wrote a memo conceding that mefloquine in some cases has been dispensed without documentation in the medical record. And that it has been dispensed without screening for contraindications. And without distribution of the product insert. So this is a remarkable concession. And we don't know, of course, which veterans that applies to. So we must assume that it may apply in any case. Without those three things then we must presume that a veteran was exposed to mefloquine even when it's not in the record. And that if exposed to mefloquine, they didn't receive any guidance or instructions or education as to under what conditions to stop taking the drug. And so if that veteran developed anxiety, depression, restlessness or confusion and should stop taking the drug, we must assume, because they didn't receive the documentation, that they continued taking it. And according to the product insert, consistently since 1989, that has

placed them at risk of a, quote, more serious event. What could be more serious than anxiety, depression, restlessness or confusion? Only very serious psychiatric morbidity or neurological disease. And now we have the FDA boxed warning which clarifies that these side effects, these symptoms of mefloquine toxicity, don't resolve when you've removed the drug and in some cases the neurological effects can be permanent. And the permanent effects the FDA acknowledges are tinnitus or ringing in the ears and dizziness or vertigo. So for any veteran with a diagnosis of tinnitus, dizziness or vertigo, that deployed to a malarious area where use of mefloquine was plausible, even if they have no documentation of that fact, they may have a legitimate claim. But more – perhaps more worrisome in terms of the numbers affected is the FDA now also says in the product insert that psychiatric symptoms may last years after use and of course the early product insert said weeks, then said months, and now they're saying years and so for all intents we must assume the psychiatric effects from the drug are also permanent. And that these effects include things such as anxiety and depression. So conceivably any veteran with an anxiety disorder or a depression disorder who had deployed to a malarious area may also have a valid claim. And the numbers of veterans that may be so affected are of course very high.

DANIEL SULLIVAN:

When you say anxiety disorders, would that include things that we generally call panic disorder or post-traumatic stress? Would they be – would they be similar anxiety disorders or generalized anxiety disorder, basically any anxiety disorder could be potentially caused by this?

REMINGTON NEVIN:

So those disorders are diagnosed based on a combination of symptoms. And there are many, many ways to put combinations of symptoms together to come up with a particular psychiatric diagnosis. It's entirely plausible that an individual suffering from the abnormal dreams or nightmares, paranoia, memory problems, and situational anxiety that may accompany chronic mefloquine toxicity, it's very plausible that even a very experienced psychiatrist might consider that consistent with post-traumatic stress disorder. And so the VA will have to determine whether a particular psychiatric diagnosis is plausibly consistent with the chronic effects of mefloquine as they are documented in the product insert and as the literature establishes them. More research is clearly needed here to be able to make a finer determination whether this is truly a psychiatric disorder that has nothing at all to do with mefloquine or whether it's a constellation of psychiatric symptoms that's plausibly related to the earlier administration of the drug. And so I think the fact that we now have claims being processed favorably by VA, I think this is going to motivate more research in this area and help us to refine diagnostic criteria for this mefloquine syndrome.

DANIEL SULLIVAN:

And one of the things that I think we're learning about exposures in the war theatre is that they may interact with one another. So a mefloquine exposure might interact with some of the other toxic exposures and it may be that somebody may be suffering from a stress associated event and a toxic exposure, rather than an either/or sort of thing.

REMINGTON NEVIN:

Yeah, that's exactly right. And I think many veterans who are suffering to some degree from the chronic effects of mefloquine, many of them may have already been eligible for disability for traumatic brain injury or PTSD and so the number of veterans that may seek out this new method of claim, it may be relatively small in comparison. But I think it's important to get a proper diagnosis and we do need to tease out what chronic effects are due to TBI, due to post-traumatic stress disorder, or maybe due to mefloquine toxicity. And some years ago in 2012, I testified to the senate that I thought that mefloquine toxicity was going to be the Agent Orange, mefloquine was going to be the Agent Orange of this generation — and that we needed to consider mefloquine toxicity as the third signature injury of these wars. And not look at any of the three in isolation, but consider the relative contribution of each. There is undoubtedly a significant comorbidity and that's not just my opinion. In numerous recent editions of the CEC's travel handbook, my military colleagues write that the effects of mefloquine can confound or complicate the diagnosis and management of post-traumatic stress disorder and traumatic brain injury. Because the symptoms are so similar.

DANIEL SULLIVAN:

Well, we're nearing the end of our segment here. And I wanted to end on a note of positive forward thinking and ask what is it that you think could change about the military health care approach that would enable DOD to better anticipate and prevent this type of injury? What could we push for as a growing movement demanding or questioning a better response to toxic wounds, better prevention for toxic wounds? What could we ask the DOD to do with respect to this particular issue? Considered broadly, the issue of medications, preventative medications and their potential long term effects? How could we address this?

REMINGTON NEVIN:

Yeah, great question. So there is one community in the military that was entirely spared the problem of mefloquine toxicity. And that's our aviators. Our aviation community was not permitted to take mefloquine. Because the early results of testing showed that it could cause dizziness and of course dizziness in an aviator is not desirable. But of course that same reasoning should apply to the average front line soldier. You know, dizziness in a sniper trying to hit a target a mile away is similarly undesirable. Dizziness in a private driving an MRAP through a narrow village is similarly undesirable. I've often wondered why we make this distinction between these very high and careful sets of medical standards for aviators and the seeming absence of medical standards for all other troops. Had we applied the principles of aviation or aerospace medicine to the much larger population of front line soldiers, we could of perhaps eliminated much of the problems that we've experienced over the past decade. Aviators receive very careful medical exams at intervals. They don't need to be evaluated as carefully before deployment because their doctors know everything about them already. Every time they start a new medicine, every time they have even a problem with their wife at home. The flight surgeon or the unit doctor needs to know about that to determine if they're still suitable for continued duty. And I think if the military moves to a paradigm of constant medical readiness, constant assessment of adherence to medical standards, we can dispense with much of the pre and post-deployment cycle which is often rushed and very insensitive and prone to error. And get a much better feel for the continued health of our service members. Of course, it has the advantage, Dan, of being able to permit much more rapid deployment. You know, someone who is already green-lighted for deployment as a result of their monthly or annual exam doesn't need to go through in the army what we call SRP. And I think the military should consider in light of the experiences of the past decade really revising its pre and post-deployment paradigm and move into more of an aerospace medicine model — very expensive. It will require many more physicians. It will require much better assessment of potentially disqualifying conditions. We wouldn't be able to get away with sending twenty percent of our force downrange on psychotropic drugs as we have been doing for the past decade. We would need to recruit fitter and healthier volunteers. But as we downsize the military and the military becomes a much more desirable career option in troubled economic times, we could do this and this would prevent I think much of the chronic morbidity that's associated with carelessly deploying unfit troops into dangerous environments.

DANIEL SULLIVAN:

Well, it seems to me based on your description that taking this model and applying it to military health care overall could lead to a much more effective, much healthier military that could – could respond to threats in a more effective way. And at the same time eliminate a lot of the suffering that has been a result of some of the kind of outdated policies that exist right now. And the Sergeant Sullivan Center is all about pushing for a reform in military health care to – and VA health care – to employ best practices for occupational health. Which we also think, and as Dr. Nevin I think just articulated, we believe it's in the best interests of our national security as well to provide the best possible health care for our nation's men and women who go to war for us and perform other military operations. It's also important for the American public to honor and recognize all of the injuries of war, traumatic brain injury, post-traumatic stress injuries from blasts and ammunition and also the toxic wounds of war, the forgotten toxic wounds of war, including what we have just discussed today, which is a toxic wound affecting many, many service members who deployed in the post 9-11 era, that of mefloquine injury. Dr. Nevin, thank you very much for joining us.

REMINGTON NEVIN:

My pleasure, Dan. It's been great to be here.

DANIEL SULLIVAN:

Thank you all for listening. We have reached the conclusion of our podcast and thank you for your support of the Sergeant Sullivan Center and its mission.

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