Airing Pain 114: You, Your Drugs, and the Law: Gabapentinoids and medicinal cannabis

On 1 April 2019, Pregabalin and Gabapentin, drugs recommended for the management of neuropathic pain, were re-classified as class C controlled substances.

Medicinal Cannabis: Is it safe? Does it work for pain? Is it legal?
Where do people who use these drugs to manage their chronic pain now stand within UK law?

In this edition of Airing Pain, contributors Blair Smith, Consultant in Pain Medicine at NHS Tayside, and National Lead Clinician for Chronic Pain in Scotland, Steve Alexander, Associate Professor in Molecular Pharmacology at Nottingham University and Cameron Rashide who lives with neuropathic pain.

Paul Evans: This is ***Airing Pain***, a programme brought to you by Pain Concern, the UK charity providing information and support for those of us living with pain and for healthcare professionals. I'm Paul Evans, this edition of ***Airing Pain*** has been funded by Foundation Scotland.

Cameron Rashide: There are people out there that have found out this is a strong drug, and want it. But people like us are struggling every day. From the moment we open our eyes to the moment we try to close them. We're not taking it for the fun of it. We're taking it to ease our body. We have to live with this pain that a normal person doesn't have to live with. So why make it so difficult for us? Why make it harder for us to go and get something that you prescribed? You asked us to take because you said it was good for us. And now you're saying it's a prohibited drug.

Evans: On the first of April 2019, pregabalin and gabapentin, drugs recommended by the National Institute for Health and Care Excellence as being effective at reducing neuropathic pain and are safe and cost effective, were reclassified as Class C controlled substances in the UK. The change means it's illegal to possess pregabalin and gabapentin without a prescription, and it's illegal to supply or sell

them to others. It also means that doctors will now need to physically sign prescriptions rather than electronic copies being accepted by the pharmacists. And pharmacists, for their part must dispense the drug within 28 days of the prescription being written. If calls to the Pain Concern helplines are anything to go by, it's a change that's made people who live with neuropathic pain absolutely furious. Cameron Rashide lives with chronic pain.

Rashide: My chronic pain started shortly after I had a car accident. And then in the same week, I fell down quite a lot of stairs. So, it just – it was like double impact on the spine. Straight away I didn't go to the hospital. So, then it was like slowly started building and got worse. So literally, I've been living with it [for] 30 years.

Evans: So how does it affect you?

Rashide: I've had to give up work, which I really liked. It literally got to the stage that I used to push through the pain and go to work. I live in East London and I was working in Richmond. So, the travelling took a big impact on me. And then when I had to give it up, that was the line of me realising [that] this is too much.

Evans: A strange question, but how does your pain feel?

Rashide: You know, when you have a can of Coke and you want to smash it? I am the can of Coke and you're smashing me. That is literally an everyday thing from top to toe.

Evans: So, you're being crushed, basically.

Rashide: Totally, every day. And not even giving me a breather in between.

Evans: So, is this neuropathic pain?

Rashide: First, I was told it was just the disc. And then it's turned into neuropathic pain. So, they realised I had that shortly after I had the stroke.

Evans: So, you've had a stroke as well. Can I ask you about your medication?

Rashide: I've been taking pregabalin for over three years now.

Evans: How does that help?

Rashide: I take it in the evening, and if the pain flares up during the day time. It doesn't delete, but it eases the pain to the point that you can relax and try to sleep. You won't have a full night's sleep but you'll have some sort of sleep.

Evans: Now they've just changed the classification of pregabalin and gabapentin, how does that make you feel?

Rashide: I'm on other prohibited drugs. So, it's like, 'Okay, am I taking too much?' This is also one thing that we learned in the group about your medication, the level of medication that we've been given. Are they going to help you? Or is it going to stop your pain? I think with it going into prohibited, you're actually making people think, 'Okay, if it's going to help them, it's going to help them.' But I've started to think, 'Am I taking too many drugs, that are going to mess me up later on in life?' Because, obviously, depending on your [tolerance], and so on, what's going to happen? Because sometimes, obviously, the doctors need to change your doses. You can up them [or] down them, so some people start relying on drugs. I'm one of these [people that believes] in alternative therapy, but I realised as well that you need to take medication when you have to take it but having it now classified – I wasn't really happy [about] that. It actually made me feel [that] I'm taking something that is a high-level drug, because you can't, now, have a repeat done. You can't ask the chemist to drop it off no more. You personally have to go to the surgery. You have to ask the doctor for it. And then you have to give it to the chemist to fulfil.

Evans: It's almost as if they don't trust you.

Rashide: Yeah. There was one time like, my GP did get annoyed and said, 'Look, she can't walk, she can't come surgery to get it. Why can't you just repeat it?' And it's like, okay, it's a prohibited drug. First of all, why are you giving out then if it's so strong? Why are you giving it on prescription, why are you giving it to anybody? If you have given it out, why are you still giving it out if you think it's prohibited? Why

didn’t you stop it before you made it prohibited?

Evans: So, let me get this straight in my own head. You have to visit your GP once a month. Now you get a month supply.

Rashide: Yeah.

Evans: And he or she has to say**:** ‘Yes, she's good for another month’.

Rashide: Yeah.

Evans: And you've had pain for thirty years.

Rashide: Exactly. So that it annoys you, because you've got to go through this every month just to pick up one medication. If you were going to do this, you should either have this register – i.e. like in America, they give you little cards. Why don't you do that with all the patients that have it already? That have got to have it? Why do they have to go through this continuous – Go to the surgery – The doctor has to check you out? All right, there are people out there that have found out this is a strong drug and want it but people like us are struggling every day. From the moment we open our eyes to the moment we try to close them. We’re not taking it for the fun of it. We're taking it to ease our body. We have to live with this pain that a normal person doesn't have to live with. So why make it so difficult for us? Why make it harder for us to go and get something that you prescribed? You asked us to take it, because you said it was good for us. And now you're saying it's a prohibited drug.

Evans: Are they saying it's not good for you?

Rashide: That’s the question. They've never said it’s not good for you. But they've classified it as prohibited.

Evans: What does your GP say about it?

Rashide: The first week it happened, when they made it prohibited. She did the mistake of giving me a six-months repeat. Okay, so she made six prescriptions up like she would do for my repeats. They were taken to the chemists to cut and the

chemist point blank refused to fill them. Then I had to go back to the surgery to pick up another prescription to be filled. So, in other words, I've gone through two different hassles. And none of the GPs that I've visited have actually commented on the way they've had to do it now. They've said, 'The law is the law.'

Evans: It seems strange to me that they're not criminalising people, but they're not just burdening you, the person who lives with pain, who needs these drugs, but they're also putting the GPs into the same box, that they can't be trusted either.

Rashide: Yeah, it is. Because it's like, who are they giving it out to? Are they giving it out the right patients? Or are they giving it to these people? I'm not one of these that always say, 'Oh, the government doesn't trust us,' and so on. But it's starting to look like that now. It's like the old saying, 'If something's working, why change it?' Doctors are wise enough not to give it to [just] anybody. They're not going to give it to Tom that's just broken his thumb. They're going to give it to Peter that's been suffering of thirty years or forty years, who has been on it for a reason. They are sensible enough, after all, they did go through medical school. The government didn't, so why are doing this?

Evans: That's Cameron Rashide. Blair Smith is a consultant in pain medicine at NHS Tayside. He's national lead clinician for chronic pain in Scotland. His research interests have been to look at the rates of prescribing of some of the drugs used in the management of chronic pain, including pregabalin and gabapentin.

Blair Smith: The reasons for its introduction are to improve the safety of prescribing at a population level, to minimise the risk of people who are obtaining the drug and taking higher doses than necessary, or people who are perhaps even diverting the drug to the streets, or to minimise the risks of the increase in drug-related deaths that have been associated with gabapentin and pregabalin. So, it's done for patient safety reasons. It isn't done to punish people who are obtaining benefit from the drug, taken for the correct indications. It's important to state, at this stage, that gabapentin and pregabalin are actually very useful drugs for treating particularly neuropathic pain. And anybody who is taking these drugs and deriving benefit from

them, for their neuropathic pain, shouldn't be concerned because they are going to continue to be available. And they are going to be able to get their drugs and the medicines when they need them.

Evans: But the chronic pain patient communities are very disturbed by this, very upset by this. Explain why.

Blair Smith: Well, I think because of the publicity that's attached to it, and because of the perceived – and in some cases – maybe actual slight increase in difficulty with getting prescriptions, I can understand that people who are obtaining great relief from their very distressing neuropathic pain will be concerned that this is going to be taken away from them. And that was really what I was meaning before: they shouldn't be concerned about that because they're going to continue to be available through the same routes as before, normally through their general practitioner.

I think there's probably also concern that, because of the publicity attached to it and other publicity surrounding the identified increased in prescribing rates, that there's a perceived stigma attached to it. They perceive that they are being perceived as drug addicts, I suppose.

Evans: It's almost like criminalising them.

Blair Smith: Yes, well, I can understand why that perception goes ahead. Certainly, there isn't that perception within the medical community and within the healthcare professional community, for whom anyone who's obtaining benefit from gabapentin or pregabalin, usually for neuropathic pain should certainly continue to get them without any problem or issue.

Evans: Are they addictive?

Blair Smith: If you read the press, there's an assumption that they are addictive, but I have yet to read any evidence of their addictiveness, and that's research that needs to be done. We've been discussing that with colleagues in Dundee. It's not even clear what the effect of them is, other than pain relief. There clearly is some effect to

make them valuable currency on the street and in prisons. We think it might be to do with potentially enhancing the effect of opioids taken at the same time. That's the – that's the theory. So, if you're taking an opioid, whether it's heroin or morphine or Tramadol, whatever, if you're taking that in order to generate pleasurable sensations, [such as] euphoria, there may be an additive effect of gabapentin [or] pregabalin [can] prolong [the effect] or [reduces] the dose of the opioid that you need to take in order to gain the same euphoric effect. But by themselves, I don't know of any evidence to say that the gabapentin or pregabalin are addictive. If you're taking a strong opioid, such as morphine, there's a thing called tolerance which often develops, which means that the effect that you have at a certain dose reduces in terms of its pain relief, so you have to take a slightly higher dose to get the same effect. And that keeps going so, potentially, you could keep having to increase your dose and then you find yourself in a very high dose and unable to come off it because a dependency has set in. I've not seen that with gabapentin or pregabalin, and I've not read any evidence of it. Once you reach the dose of pregabalin that is most effective for your pain, then that dose can remain stable, with the same effect, for long term.

Evans: Professor Blair Smith. Well, Pain Concern publishes its own leaflets, written by leading experts, on how to manage your medications for chronic pain, including one specifically on pregabalin and gabapentin. You can download it from Pain Concern's website which is painconcern.org.uk and from there, you'll also be able to listen to all 114 additions of ***Airing Pain,*** and also find details of our magazine, ***Pain Matters***. Now, another drug that's creating its own media frenzy over its legal status for medical use, is cannabis. Steve Alexander is Associate Professor in Molecular Pharmacology at Nottingham University.

Steve Alexander: In particular, I've been interested in cannabis-related medicines and cannabinoids for about twenty years. And of course, that's relevant to pain because of the overlap in the use of cannabis in many areas the world, and the hypothesis that endogenous cannabinoids can maybe regulate pain mechanisms.

Evans: Well it's very apt as well because cannabis and cannabinoids are hot stories

in the news at the moment. Now, tell me what is the problem with using cannabis for pain-related [purposes]? If there is a problem?

Alexander: There are several issues. The first one is legality. Clearly, we're in a situation where only very recently has there been a move to move cannabis-derived medicinal preparations out of schedule one. I should point out that cannabis, itself, is still schedule one in this country. But what has happened in November was the move to schedule two licencing for cannabis-derived medicinal preparations.

Evans: Just explain that schedule one and schedule two. What the difference is and do they govern what the public can do or what the professionals can do?

Alexander: So, scheduling has been around since the ’50s. And different countries have slightly different versions of it. But essentially, as derived by the United Nations, a schedule-one compound would be something that has no medicinal value. So aside from raw cannabis, compounds like LSD, and MDMA, are described as schedule one. Where, at the moment, there's no perceived clinical benefit. Lower levels of scheduling, describe drugs which should be controlled, where there is a potential for abuse, for example, but where there is medicinal value. And so, the schedule level is meant to reflect the sort of severity of potential damage or diversion or abuse that could be associated with those. It's kind of a difficult one because we know that illegal cannabis is very widely consumed in this country. But it still remains a scheduled drug.

Evans: I do know people who use illegal cannabis, who smoke cannabis, who swear that it is very good for managing their chronic pain.

Alexander: There is, as you say, an awful lot of accumulation of anecdotal evidence. And it's a difficult one to, you know, if you come from it from the scientific clinical aspect, you want to see clinical trials where things are done in a rigorous, side-by-side manner where you can point to a clear difference between people who have the active ingredient and people who don't have the active ingredient and see that it's a positive. And there have been a lot of those sort of clinical trials conducted in the past. If you look at the sort of meta-analysis, there is a benefit [of cannabis] to be

had in pain. It's not huge. And I think the reason for that, which we can come back to in a second, [is that] I think individuals who see that benefit – you can understand that they're willing to break the law. For chronic pain sufferers, if their alternative medication, their existing medication, isn't doing the job, I absolutely empathise with them about [their] need to break the law.

Evans: Empathy is perfectly understandable. But the fact is that cannabis, raw cannabis, street cannabis, has its dangers as well.

Alexander: Absolutely. So, there are two issues I have with illegal drugs. And the first is that they are illegal and the second is there is no quality control. So, you don't know what you're getting. Even if you go back to the same individual, you will be getting things which vary quite a lot. And what we also say, you know, it's not just that there is a change in the sort of content, the high levels of THC that people would describe as ‘skunk’, but there's also occasional levels of adulteration**:** people using synthetic cannabinoids and adding them to cannabis, and that can be potentially dangerous as well. So, although it's not overtly life threatening, doesn't mean it's safe. So, THC is, I suppose, the most famous cannabinoid, so the cannabis plant is wonderfully rich in its diversity. It's got over a hundred – what appear to be – unique metabolites to that plant, and we still don't understand why. It’s an interesting sort of facet of botany. But the one that is regarded as the major psychoactive entity in terms of giving the high that non-medicinal users want, appears to be THC: tetrahydrocannabinol. So that's also effective in terms of delivering analgesia but the downside is it produces this dissociation from the environment, hyper-locomotion, so people go into a sort of – not a catatonic state because it's not quite that, but short-term memory loss, impairment of some of the visual ideas as well. So clearly, if we're wanting people to be functional, and to have pain relief, then that is far from ideal. And so that has been an issue about the use of cannabis.

One of the things that is kind of interesting is trying to figure out, if you can choose a dose that might be beneficial in terms of providing pain relief, and not being too bad in terms of removing you from your environment, that's proving a little bit difficult because of the way in which people take cannabis. So, smoking is by far the most

common way that people take non-medicinal cannabis. And with that, you can do a little bit of titration, because there's a relatively short delay between taking a hit and feeling those sensations. But clearly that's not something you can promote as a mechanism for treating an illness. So, the alternative routes of oral administration are very slow, in terms of onset; these are not very well absorbed compounds. And so, getting the right dose for an individual is actually quite difficult. And that's one of the sorts of things that I think would really help, would be to have a bit more precision about the delivery of these agents. So that the places in the world where medicinal cannabis is available and where you do have quality control and reproducible levels of particular cannabinoids in those preparations, they often try and personalise it and personalised medicine is great. It's one of the things that we're trying to advocate for people in general. It's really nice to be able to identify that people are different, they respond very differently in the ways in which they handle the drugs and the effects. So, it's nice to have that personalisation, but it's a really difficult one to start off with, if you like. So, with an established medicine, to look at how people are different in their responses, and then pick those who are much more likely to respond, is kind of the accepted way of doing it. But starting off with something which we know is quite variable, and then trying to pick people who are going to be better responders and people are not going to respond as well – that's not as straightforward. So often what goes on in the other countries where medicinal cannabis is legal, is that they start off with low doses. So, it's the sort of tradition, ‘Start low, go slow,’ and vary the dose and sometimes vary the content, so the THC that we know provides some analgesia – you kind of try and ramp that one up until a time where the patient feels they get the optimum benefit.

Evans: Now you're talking about cannabinoids and cannabis. What is a cannabinoid?

Alexander: Cannabis is the plant. We've had versions of cannabis in the UK for hundreds of years. We've used it over many years as a source of fibre. So, in the Elizabethan era, it was grown and, in fact, if you had a particular size of land, you had to grow hemp for the rope and sail that was used in the Royal Navy. But that

was very low in the cannabinoids. So, it didn't have the high levels of the active ingredients that we talk about in terms of the medicinal properties. As with most plants, there is a huge variation depending on the seed that you use in the first place, how you grow it, where you grow it, how you harvest it, how you store it, and all those sorts of things – which parts of the plant to use as well. Cannabinoids were often called secondary metabolites. They're not actually needed for the basic metabolism of the plant, but they accumulate and they might be something to do with the plant's own immune system, because there's a story that maybe it reduces parasitic infection of the plant itself, and so they thrive. So, these accumulate particularly in the female buds, some people have listed maybe 114 of these which seem to be relatively unique to the cannabis plant, and those are the things that have been associated with things like religious practices in India and the Caribbean. And then the sort of abuse, if you like, this street use that we think of primarily when somebody says 'cannabis' to you.

Evans: In terms of legality in the UK anyway, you can buy cannabis oil on the high street. So, what is that?

Alexander: So that's primarily derived from the seed. So, the legality of the situation is that they should not contain above a certain measure of THC. So, the principle is that they're obtained from versions of the plant which maybe have a low THC content, the derivation of the oil is as much as you would [derive] from any seed, it's kind of a pressing process, and the oil is extracted. Many of these contain one of the other cannabinoids called cannabidiol. A compound which is very interesting in terms of treating childhood epilepsy. So that particular agent of purified cannabidiol has recently been approved in the United States for treatment of particular versions of infantile, intractable epilepsy. So, [for] kids who just don't respond to normal medication, and have forty/fifty seizures a week – horrible. And in some of those [cases], not all by any means, but in some of those cannabidiols seems to reduce that to something which is manageable.

Evans: And these are the stories that are making the headlines at this moment.

Alexander: So, as you're probably aware, last spring and summer, there was quite a major sort of campaign highlighting a couple of incidences in the UK, where kids who have this disorder, were being treated up to a point with versions of cannabinoids, mainly cannabidiol. Which – [it's] very difficult to know for sure what the content of those things were. But yeah, that became such a high-profile [campaign] that I think that prompted the politicians to look at the situation and ask the scientific clinical community to re-evaluate kind of striving into some preparations and that prompted the change in the law. Because there are so many different metabolites, we've really got good information on the two, THC and CBD: tetrahydrocannabinol and cannabidiol. But the others – we're beginning to identify that they do have bioactivity. Whether that's useful or not, we don't know. Some – most of the medicinal cannabis producers focus on those because we've got good evidence that they may have useful effects at the right doses. And then, because they're relatively minor metabolites, the others, they kind of leave them to one side. But we're beginning to appreciate that they may have beneficial effects as well. I think one of the other things to say is that, quite often, drugs are not given in isolation. And obviously with an elderly population, as people grow older, they accumulate more issues, and so it's much more common for them to have combinations of medicines. The overlap between how drugs might be metabolised by the body, and the potential interactions that might happen, is clearly an area that needs clarification with co-administration of many medicines.

Evans: Let me clarify this in my own mind. The THC that is not – or [is] at very reduced levels, in the cannabinoid oils and things like that: that's the substance that gives you a high, in illegal cannabis.

Alexander: So, to the best of our knowledge it's the primary psychotropic agent, the mood-altering agent in cannabis. Because of its prominence in terms of our understanding of it and the abundance in the plant, it's the one that we focus on the most. It's not impossible that some of the others have some minor effects. But we don't worry so much about them because they don't accumulate in the same ways as THC.

Evans: Just for people who are totally confused by this cannabis/cannabinoid thing. Should they be nervous of going into a health food shop and buying cannabinoid oil?

Alexander: I think the evidence that we have so far is that there is not a level of consistency about the components – the constituents – that are around. I think for the moment, it's still not subject to the regulation that would allow a sort of consistency of content.

Evans: That's Steve Alexander, Associate Professor in Molecular Pharmacology at Nottingham University. Now, this edition of ***Airing Pain*** is being recorded in May 2019. Guidelines do change so please do check them. But the current NHS England guidelines for the use of medical cannabis say that many cannabis-based products are available to buy online, but their quality and content is not known. They may be illegal and potentially dangerous. Some products that might claim to be medical cannabis, such as CBD oil or hemp oil, are available to buy legally as food supplements from health stores. But there's no guarantee that these are of good quality or provide any health benefits. I'll just add to that, that whilst we in Pain Concern believe [that] the information and opinions on ***Airing Pain*** are accurate and sounds based on the best judgments available, you should always consult your health professional on any matter relating to your health and well-being. He or she is the only person who knows you and your circumstances and, therefore, [the one who knows] the appropriate action to take on your behalf. Well, I don't want you to leave this edition of ***Airing pain*** under a cloud of gloom and doom. There's more to the management of chronic pain than just drugs, legal or otherwise. So, in the next edition of ***Airing Pain***, I'll be exploring neuropathic pain. And how self-management techniques learned through a pain management programme can turn your life around. I leave you with Cameron Rashide, who spoke at the start of this edition of ***Airing Pain.***

Rashide: Before I started this group, literally it was hospital-home, hospital-doctor, hospital-home. In the last eight years, I literally stayed at home because the pain is too much for me. I stopped going out to coffee shops and wouldn't go out shopping on my own – everything online. Now, [the group has taught us] to practically do

something outside the house. Last week, my weekly goal was to go to a coffee bar. And I did that – even though I was uncomfortable, I was in pain, but it was enough to pace myself, but not overdo it. So, it's little goals, but achievable goals.

Contributors:

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- Dr Steve Alexander, Associate Professor in Molecular Pharmacology at Nottingham University
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