

***Airing Pain* Programme 101: Persistent Post-operative Cancer Pain**

This edition is funded by The Agnes Hunter Trust.

An ever-increasing cancer survivor rate means chronic pain associated with the condition and its treatment is growing. In the UK alone, cancer survivor rates have doubled in the last 40 years, from 24 percent to 50 percent.

*In this edition of **Airing Pain**, Paul Evans speaks to Dr Paul Farrquahar-Smith, consultant in anaesthesia and pain medicine at The Royal Marsden Hospital in London, and co-author of *Pain in Cancer Survivors; filling in the gaps*.*

Dr Farrquahar-Smith explains how post-surgical pain in cancer survivors can be caused by damage to the nervous system, what cancer treatments may be associated with this pain, and what pre-surgery steps can be taken to reduce it.

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 health care professionals. I'm Paul Evans, and this edition's been funded by the Agnes Hunter Trust.

Paul Farrquahar-Smith: What people quite often think is, because they had pain when they had the cancer, they now have pain after surgery: that must mean I've got the cancer come back. Now, in *most* cases we do not need to have the cancer coming back to explain this pain. The teams will investigate as they see fit, and they will decide whether or not, oncologically, there's an issue. But I say: look, it doesn't have to be an oncological issue. Ninety-nine times out of 100 these sorts of pains are not from recurrence. Going through and explaining what it is and what it is not, people say, 'thank you for that, because I didn't know.'

And people are saying to me, 'how can you have pain two years after surgery? You should be back on your feet, back to work, and everything should be rosy.' What we do though is [that when] you look at people who've had head and neck surgery – had major neck dissection after head and neck surgery – *two* years after, 75 percent of people have *not* gone back to work, because of symptoms from many things, including pain.

Evans: One of the consequences of our ever-increasing cancer survival rate is that the number of people who experience long-term pain as a result of the cancer or its treatment is growing. A recent review, 'Pain in Cancer Survivors - Filling in the Gaps' by doctors Paul Farrquahar-Smith and Matthew Brown states that, clearly, cancer treatments – new and established – can be associated

with a significant long-term pain burden, and that time and resources must be invested into understanding and consequently treating what is a growing pain epidemic.

Dr Paul Farrquahar-Smith, one of the authors of that report, is a consultant in anaesthesia and pain medicine at the UK's leading tertiary cancer centre, the Royal Marsden Hospital in London. He treats both in-patients and out-patients, where he sees, predominantly, cancer survivors who live with long-term pain.

Now, this might be a silly question, but rather naively I would have thought that the word 'survivor' in this context is someone who's had cancer, been treated successfully, and is therefore better. So how does he define survivor?

Farrquahar-Smith: Well, our working definition is that [a survivor is] anybody who's been diagnosed with cancer and is still alive. Now, that pools in a number of different populations: those who are actively going through current treatment; those who have recently stopped treatment, and those who maybe had treatment years ago, and yet are still having issues with some of the symptoms from the treatments, or other things.

Evans: The word survivor conjures up a very small number of people who survive with disaster. Cancer isn't a disaster anymore.

Farrquahar-Smith: Yeah, there's been discussion about the use of the term 'cancer survivor' and whether or not it has negative connotations because of the use of survivorship. I think it sort of works to a degree, but that doesn't mean we should allow it to carry on – maybe if there's a better term somebody can come with, then great. But, for me, I think people *do* like the fact that they have survived; they have vanquished something; they have succeeded. Although we've got to be careful not to say that people who don't survive are failures or – what do people say? – 'you've lost your battle.' It's not about battles, it's about surviving the best we can. And I think, at the moment, it *does* encompass the group of patients we see, and most people *do* refer to themselves as a survivor – as I've said, with that caveat that there probably are better terms if we thought about it. But it's still commonly accepted as being the term to use.

Evans: But the title of your research paper, 'Pain in Cancer Survivors' – survivor doesn't mean that the treatment is over?

Farrquahar-Smith: No, not necessarily. Again, it does depend on what definition you look at. But the working definition is that anybody who's been diagnosed with cancer and is still alive, to me, is a survivor. And also it reflects that we do see people at different stages in their cancer journey; it doesn't mean that we're only dealing with people who've had their treatment and are now in remission or cured. No. Although that *is* a group of patients that we see, we include everybody else in that because we treat those people. For example, if people with procedure pain – acute pain that they have [which is] associated with the treatments they have, which are surgery, chemotherapy

and radiotherapy.

Evans: Well, I was going to ask you: what are the causes? One might assume that following treatment for cancer – successful treatment for cancer – one might assume that there would be no pain there. So what does cause that?

Farrquahar-Smith: The main avenues of treatment are surgical, radiotherapy and chemotherapy. Now, each of those treatments have symptoms. The one we see a lot of is post- or after-surgery persistent pain. Now this is a very strange concept to people who don't know – and even to some practitioners – because this is where pain persists, even though the surgery may be healed and, to all intents and purposes, done and dusted.

However, there is a significant proportion of patients who get significant pain after their surgery for reason that aren't apparent if you don't know them. And they are what happens to the underlying nervous system. Damage to the nervous system somehow creates a situation where it maintains the pain itself without having to have the damage to maintain it. So this is this persistent post-surgical pain that you can get after any sort of surgery – not just surgery after cancer, but any sort of surgery – and it's a very common problem nationally. We see that a lot especially after breast surgery, especially after head and neck surgery, especially after thoracotomy, which is cutting the chest for certain procedures: some lung procedures and some gastro-intestinal tract tumour procedures.

Evans: Just explain what's going on there – the affected part has been removed, and the cancer has been removed, if you like, but the pain – or a different sort of pain – persists?

Farrquahar-Smith: Yeah, so what happens is people get an acute pain, a pain around the time of surgery, which we understand, we know we can do things about, and is generally pretty well done. What happens is, because of a change in the nervous system, the pain sensing system gets set up so normally when pain is caused it's caused by tissue damage. But then this pain takes over and the pain is the problem in itself, and it's *not* caused by tissue damage – although that would originally have been set up, we think, by damage to nerves you can't see at the time of surgery. So it's like, the collateral damage is unavoidable to get rid of the tumour, but then that sets up changes in the nervous system that then causes this pain that can carry on without any external influence.

And this is this persistent post-surgical pain which is very problematic and difficult conceptually, because people say, 'look, how can I have pain when everything's healed up and everything's gone?' And this is this change in the nervous system that is set up that then causes the maintenance and perpetuation of the pain.

Evans: So is that what they call neuropathic pain?

Farrquahar-Smith: It is thought to be a *type* of neuropathic pain. So neuropathic pain just says that

it's pain probably from damage or a problem with the nervous system. That's quite a broad spectrum. But this pain is thought to be one of the sub-types, if you like, of neuropathic pain – or *predominantly* neuropathic.

Now, without getting too complicated, there are definitely some patients with this persistent post-surgical pain that don't seem to have very many neuropathic elements – the pain doesn't sound, isn't described in the ways neuropathic pain normally is. However, we do think that predominantly it is neuropathic-y, or neuropathic-like in certain cases, and therefore the current treatments do tend to be based around our current treatments for neuropathic pain.

Evans: Which are?

Farrquahar-Smith: Well, there's many. There's the non-pharmacological: supportive care is also very important; psychology, physiotherapy; all these are very important things. We tend to also sort of use pharmacology and then the pharmacological ways of addressing neuropathic pain, which are many different types of drug, which include those medicines which were previously known as anti-depressants and anti-convulsants. Now these are a bit of a misnomer, because these medications are not being given for depression nor are they being given for epilepsy. However, the mechanism that they work or used to work – or drugs like them used to work – for depression and epilepsy are the same mechanisms that are important to try and reduce the pain in neuropathic pain. But it is a misnomer and they probably shouldn't be called that; but that's how they're commonly known.

Evans: The best way I've heard them described is [that] they calm down the nervous system; is that right?

Farrquahar-Smith: Again, without getting too technical, the anti-depressants are thought to reduce this pathway which is the descending excitation. So the way the pain goes from the periphery into the spinal cord into the brain, it has several points at which that pain signal is modulatable. And one of the modulations comes from the brain: so the brain has these descending pathways, both excitatory – i.e. switching on – and inhibitory pathways – switching off. What the anti-depressants do is affect those descending pathways. One way of doing that is reducing the descending excitation and the other way is increasing the descending inhibition. And it's thought that it does a combination of these things.

The anti-convulsants tend to have a slightly mechanistic way of operating, in that the ones that are most commonly used, which are the gabapentinoids, which are gabapentin and pregabalin, they act by reducing the activity at the level of the spinal cord. So they directly reduce that transmission, if you like, the electrical signal, by reducing the effect of the normal transmitters on the normal system. So it calms the system down. Now, that's how we think it works but there are other things that can be useful.

With these medications are secondary effects. For example, with pregabalin, it has an effect on

anxiety and therefore – again, not saying that the pain is from the anxiety per se – but we do know the psychological effect of pain is very important, and we can't treat the pain in isolation. So if you're also getting somebody who's got anxiety issues as well as pain then you can get a secondary effect from the pregabalin, for example.

Evans: Now, the gabapentinoids, if they reduce anxiety – and I'm thinking of things like amitriptyline, which is an anti-depressant – I know from experience [that] one of the great effects, so far as I'm concerned, is sleep.

Farrquahar-Smith: The anti-depressants, and specifically meaning medicines such as amitriptyline and nortriptyline, which is a close cousin of amitriptyline – those effects on the neuropathic pain are *independent* of the effects on depression. There's no evidence that, at the doses they use for neuropathic pain, they have any effect on depression.

However, there is a suggestion that they do have a beneficial effect on sleep. The only problem with that – with the amitriptyline and nortriptyline – is that it doesn't seem to improve the *quality* of sleep. It may be, say, that people are sleeping longer, but if you look at the quality indicators of sleep like REM sleep, etc., it's not necessarily that good. So it is a slight issue with that, and with the use of them just to try and help sleep. Now, is some low-quality sleep better than no high-quality sleep? I don't know, but it just has to be borne in mind that it's, you know, they're not perfect. But, again, when we use these medications, the anti-depressant medications, we're using them primarily for the anti-neuropathic pain effect.

Now, we have got millions of years of conditioning to say, 'pain means damage.' Because that's originally what it was there for. What we've had a growing awareness and understanding of in the past 15-20 years is that we don't need a cause for pain. Sometimes the pain is in the primary sensing system itself. And actually the new ICD [International Classification of Diseases] classification codes have taken that into consideration. Before it was always, 'pain is secondary to something else: pain caused by this; pain caused by that.' Now you can have a diagnosis of pain without any need for secondary consideration. So why have you got chronic pain? 'Because I've got chronic pain. My chronic pain *is* the problem. My chronic pain is the fact that there's an issue with my primary sensing system, and that has gone off kilter.' And *that* is why you have chronic pain.

Now, that's not for all chronic pains, but it accepts that there is an entity where pain is the issue. And that goes back to people saying, 'my pain is worrisome and serious because I think it's indicative of damage processes going on.' Now, in *many* chronic or persistent pains there is no damage process going on. For example, if you do MRI scans on 100 people, you will find a significant number of people with degenerative disease. You can do that on a hundred people who have no pain and you will find the same number. Just because you've got somebody with pain, you do an MRI scan and say, 'Ah! You've got a degenerative disease: *that's* why you've got pain' – that correlation is very, very tenuous and not really there, because you don't need it to be there.

When I see people and you look at their MRI and think, 'that looks horrible, you know, everything's falling apart,' and [yet] they have no pain. And see others where the damage may be trivial and they've got intractable, serious, very difficult pain to treat. So this cause and effect isn't clear for persistent pain.

Now this slightly – persistent pain and chronic pain, there are lots of different types, and that does change slightly depending on what you think the cause is: is the cause actually persistent pain or is there – for example, in this hospital – is it because you've got a tumour growing into your spine that is very clearly affecting the nerve and very clearly causing the problem? But even in our patients here you will see scans where you think, 'that's just terrible, they must have huge amounts of pain,' and they *don't*; and other people where you think those changes are modest and [yet they] have huge amounts of pain.

Pain is not always discernable by scans. And this is one of the things patients always say – 'people don't believe I've got pain, or don't understand how I could have pain, because I've been treated. I had my surgery two years ago; how can I have any pain after that?' And this is all part of that persistent, post-surgical pain that is set up and causes pain without any obvious reasons for it apart from what we know, and we have quite a lot of science background now to understand some of the mechanisms that are going on to cause this pain.

Evans: Well, on that subject: *who* is at risk?

Farrquahar-Smith: There are risk factors that are associated with these persistent post-surgical pains, and, again, I know we're concentrating on surgery, but we mustn't forget the chemotherapy, which, again, is our area of specialty in this hospital, and also, to a lesser degree but also important, radiotherapy.

But, to go back to people who are at risk: depending on the surgery there are different risk factors. So these are people who, if you have these risk factors, you're more likely to then develop this persistent pain. One of the things is if you have pain at the time of surgery – so that's quite interesting because that's something we can do something about. If we can reduce the pain around the time of surgery we can reduce the likelihood that that pain will then generate into the persistent pain.

Other factors that are, again, slightly different depending on the type of surgery people have are age and female sex or male sex – again, depending on the type of surgery – and also things like anxiety and depression around the time of surgery. Also chemotherapy is a risk factor; having surgery as well as chemotherapy, that's a risk factor. And there are several other, less important risk factors. But we can, to some degree, predict those people who are [at] higher risk of developing this persistent post-surgical pain. And some centres – and we're doing it to a degree – to try and single out and make sure we follow-up these patients.

We also follow-up every single patient that has been treated with pain relief medicine to, sort of, make sure they're not lost to the system – they don't get put on pain relief medicine in perpetuity. So we see these so-called transitional patients to make sure somebody follows them up after their surgery when we know they've had some kind of persistent pain, and see whether or not that pain will continue after a three-month point. Three months is arbitrary – people can get pain from surgery all the way up to three months – but it just shows that we know that there is a proportion of patients that will have pain, and that will dissipate to that three-month period. And then there is a subset [where pain] will persist more than three months. And then they can persist for any length of time.

Evans: So for people who have that pain before surgery, do you have the time and space, if you like, to treat that pain with all the psychological therapies and whatever?

Farrquahar-Smith: Yeah, it is challenging, but I think we are lucky enough to have the resources to do that, and we're lucky enough that hopefully it gets flagged up and we can do it. Now, it's not clear whether the pre-operative pain *is* a risk factor; if you treat it then it becomes less of a [factor]. What are the factors that are responsible for having that pre-operative pain, then also the factors that will make a higher risk of developing the persistent pain? It's difficult to know. It's not been clearly shown that if you treat the pain pre-operatively it actively helps; that doesn't mean we shouldn't; doesn't mean people won't get [a] benefit from that, because we're hopefully reducing their pain burden before they have to go through their operation.

And there's the psychology – again, we try and access that when we can. Now, obviously we won't see everybody in enough time before they have their surgery because of the nature of cancer surgery being, sort of, fairly quick. But we do try and flag up anybody who has pain issues beforehand to then deal with them in the perioperative period – i.e. around the time of the surgery – and then if there's any issues to follow up with them afterwards.

Evans: In the post-surgery pain, how severe is it? What sort of pain are we really talking about?

Farrquahar-Smith: Well, again, the severity is difficult to measure and we use imperfect tools but ones that are reproducible and sort of have meaning, and that's the numerical scoring. The numbers suggest that up to about 50 percent of patients can get some sort of chronic or persistent post-surgical pain, and *about* – again, slightly dependent on what papers you read, and what definitions you use – probably about ten percent will get a pain that is above five on that numerical rating score of 0-10. So that's about ten percent – and that estimation may be conservative in some people's eyes and excessive in other people's eyes; it's ballpark – that number of patients are getting severe (defined by over five on that 0-10 scale) pain persistently after surgery.

It's *usually* in the area where you've had the surgery, although it can be, sort of, referred in some areas as well. It's usually, again, mostly – but with that caveat I said that not everybody has neuropathic-type pain – that neuropathic-type pain which is said to be more bang for you buck; i.e. it

seems to be more painful even at a given level and more intrusive and more interfering in everyday activities and quality of life. So they're the features of the pain from this post-surgical aspect.

Evans: So, what long-term management do people with pain after cancer surgery or cancer treatment have? Is it a long-term thing?

Farrquahar-Smith: Yeah, well it usually is a long-term thing. Now, the natural history of how the pain goes is very difficult to piece together, but it does seem that over time things can improve; albeit [they] take a long time. The treatment is multi-disciplinary: you cannot treat pain in isolation, you have to look at all the psychology, the occupational therapy, and all these sorts of things. Which, again, we do especially in chemotherapy-induced pain, which is *a bit* different from the surgical-induced pain; it is even more neuropathic, as you might expect, because the nerves are being damaged by the chemotherapy. So we have all of these allied, non-pharmacological things working on a sort of holistic basis, if you like, and dealing with daily living, quality of life, etc.

And then we also have pharmacology, so the medicines and tablets. And we use a lot of topological approaches, i.e. putting things directly where the pain is – and the idea is that you can concentrate the effect locally without risking the medicines being absorbed around the body and causing adverse effects.

Evans: That's Dr Paul Farrquahar-Smith, consultant in anaesthesia and pain medicine at the Royal Marsden Hospital in London. As always, I want to remind you that whilst we in Pain Concern believe the information and opinions on *Airing Pain* are accurate and sound based on the best judgements available, you should always consult *your* health professional on any matter relating to *your* health and wellbeing. He or she is the only person who *knows* you and your circumstances and therefore the appropriate action to take on *your* behalf.

Don't forget that you can download all editions of *Airing Pain* from Pain Concern's website which is www.painconcern.org.uk, and there you'll also find Pain Concern's extensive resources to support living with chronic pain.

Well in this edition of *Airing Pain* we're looking at issues surrounding persistent post-surgical pain. Here's Dr Paul Farrquahar-Smith to finish this edition of *Airing Pain*.

Farrquahar-Smith: Even though the awareness of this issue has increased over the years, and now people are much more understanding – indeed, on our consent forms it actually has persistent post-surgical pain as a risk of the surgery they're having, so it's acknowledging that this is a real entity. But people still don't understand, and understandably don't understand: how can you have pain when everything's healed? And part of what we do and I think is beneficial – and we get feedback from the patients saying, 'thank you for telling me that, because now I don't feel alone, I have some idea of what's going on' – is *explaining* the concept of this post-surgical pain; what it is, and what it is not.

What people quite often think is, because they had pain when they had the cancer, they now have pain after surgery: that must mean I've got the cancer come back. Now, in *most* cases we do not need to have the cancer coming back to explain this pain. The teams will investigate as they see fit, and they will decide whether or not, oncologically, there's an issue. But I say: look, it doesn't have to be an oncological issue. Ninety-nine times out of 100 these sorts of pains are not from recurrence. Going through and explaining what it is and what it is not, people say, 'thank you for that, because I didn't know.'

And people are saying to me, 'how can you have pain two years after surgery? You should be back on your feet, back to work, and everything should be rosy.' What we do though is [that when] you look at people who've had head and neck surgery – had major neck dissection after head and neck surgery – *two* years after, 75 percent of people have *not* gone back to work, because of symptoms from many things, including pain.

Evans: I know I was speaking to a relative of mine a few months ago who had a throat cancer, and his wife, who is a health professional, was saying, 'the procedure to get rid of the cancer was excellent; nobody warned us about the recovery after it.'

Farrquahar-Smith: I can't comment, obviously, on that case, but I can say that that would be very unusual to happen in our establishment, because – as I said – already that consent [form] has that in in our surgeries. And people are aware of it, partly because I've been banging on about it for years, and people do understand it; they know that it's an issue. So, hopefully, that would not happen in our hospital because we'd be aware of it and people are coached and counselled.

Now what it is not easy to quantify is the fact that at the time you're having your surgery, you've been given your cancer diagnosis: your head is not really with it. And you can be told a whole ream of information that you do not recall. We have to understand, and it's beholden on the practitioners to make sure at the most difficult time, when they [i.e. the patients] are not processing information in the way that they normally would because of the huge impact the diagnosis has had on them, that we make sure we get over to them: 'look, surgery is one step; the journey is longer. We will support you through that journey, but it will be a long journey; it won't be a few weeks after and you're feeling back and rosy' – although that's what we're aspiring to – but we have to be aware that for many people the journey will be longer. But as long as we can support and get people through it, and to some extent identify those people who are going to have an issue, then we can get onto it quicker and safer, and hopefully get people sorted out better.

But there is a definable issue that was highlighted by the government a few years ago, is that who is looking after these cancer survivors? Now I'm moving into the group that had been cured or in remission that aren't really being seen regularly by the oncologist because there's no need for it, because the cancer's in remission, yet still have significant symptom burden. Who is looking after those patients? And we know that the cancer survivorship population is increasing, and increasing

hugely, and will be many, many millions of patients in the next 10-15 years. So there's a growing number of patients that we expect will have symptom burden for long-term after their treatments. And it's not clearly who exactly is going to give them support.

Now, we obviously are doing our best, being a cancer specialist centre. However, that's not going to be the case nation-wide. So where are these patients going to get support and benefit from? The government did write a paper about ten years ago that had a very nice way of dealing with it in the community, having that pyramid thing where you can self-refer; however, as far as I understand, there's no clear structure where that can happen, or who can supply that, because it's going to put a large burden on primary care. And unless we recognize that it *is* going to increase and have a plan going forward, it's going to perhaps become more difficult to deal with.

Evans: So patients and their supporters and their family need to know about these concerns at the start of their cancer journey?

Farrquahar-Smith: Yeah, and I think – certainly in my experience – the information is much more widely out there, the patients are being coached a lot more about these long-term issues and how they can get support, and what things we can do about it. My role, if you like, in this establishment in the past 20 years has been doing that. And people with chemotherapy and radiotherapy, it's not incurable. We can symptom control; we don't do anything about the underlying nerve recovery, but we can try and help the symptoms until the nerves, maybe months, years down the line, start improving. And, again, in the past 20 years that's improved exponentially.

So now we're seeing nearly everybody who I think has these issues. Is that so well done in other hospitals? I can't say, but given the education that we've had to do here – the things we've been doing both in publishing and in meetings and conferences – is try and highlight the problem. Not only to the public, but to practitioners. Many years ago I would get referrals saying, 'this patient's got pain, everything's healed up after surgery, I don't understand why.' And you go, 'well you should know why, because it's persistent post-surgical pain.' And now I don't get those messages anymore; I get the referrals, saying: 'I think this is post-surgical pain.'

Contributors:

- Dr Paul Farrquahar-Smith - Consultant in Anaesthesia at the Royal Marsden Hospital London, and co-author, with Dr Mathew Brown, of **Pain in Cancer Survivors; filling in the gaps.**

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