Episode 175: Healthy moves: Exercise for cancer patients, and insights into arthritis

VOICEOVER
Welcome to Up Close, the research talk show from the University of Melbourne, Australia.

DYANI LEWIS
I'm Dyani Lewis. Thanks for joining us. The benefits of exercise have been known since antiquity and with industrialised nations around the globe facing increasing rates of obesity and diabetes, messages warning against a sedentary lifestyle are hard to miss. Joining us today on Up Close are two young researchers who are exploring different aspects of physical movement as part of their doctoral studies here at the University of Melbourne. Later in the program we'll be talking to Tommy Liu about arthritis, a multi-faceted condition that affects the mobility of millions globally. But first we are joined by Catherine Granger. Catherine is a physiotherapist undertaking her doctoral studies at the University of Melbourne's department of physiotherapy. Regular physical exercise has been shown to prevent everything from obesity, to heart disease, to type 2 diabetes, diseases that are becoming huge problems in both developed and increasingly in developed nations. But what role can exercise play for those who are struggling with a life threatening illness? This is a question that Catherine is looking at in her PhD. She's looking at exercise in patients diagnosed with lung cancer. Welcome to Up Close Catherine.

CATHERINE GRANGER
Thank you Dyani.

DYANI LEWIS
Now Catherine I imagine that getting a diagnosis of cancer is really the sort of thing that would put something like exercise pretty low down on the priority list, but what is our state of knowledge about exercising cancer patients?

CATHERINE GRANGER
Over the last 20 years or so there's been a lot of research looking at the benefits of
exercise, or higher levels of physical activity, so for example, walking to work or walking up and down stairs and that sort of physical activity for people with a cancer diagnosis. And most of that research has been performed looking at patients with types of cancer such as breast cancer or colon cancer or colorectal cancer and we know have some very strong evidence to show that exercise is very beneficial for those patients. For example, exercise can improve your fitness levels, your physical function, so your daily activities such as how easy it is to stand up from a chair and have a shower and do things like that and also your quality of life, and factors such as mood and depression, so we have a large amount of evidence which shows that exercise is very beneficial in the general cancer population.

DYANI LEWIS
If we turn then to lung cancer specifically, I mean what is the general treatment regime for lung cancer patients?

CATHERINE GRANGER
So for people with lung cancer, it depends on exactly where the tumour is and the stage of the disease so how progressed the disease is. But often people with lung cancer will go through a form of treatment such as surgery to resect the tumour, then followed by a period of chemotherapy or radiation therapy. All those types of treatments have very significant side effects to the individual.

DYANI LEWIS
And so tell me about the study you're working on. Who are your participants and what are you trying to measure?

CATHERINE GRANGER
We are looking at people who have just been diagnosed with the type of lung cancer called non-small cell lung cancer and that's the main type of lung cancer diagnosis. We are inviting people to be part of the research right at the time they're diagnosed, before they go through any type of treatment and our research is looking at how physically active people are, when they're diagnosed with cancer, with lung cancer in particular and what their fitness levels are like and how strong their muscles are and their quality of life. Then we're following patients as they go through treatment and during the disease, following up six months post diagnosis to understand how these factors change and how they interrelate with how much activity people may do.

DYANI LEWIS
So how are you measuring some of these things, like the level of fitness or physical exercise that the patients are doing?

CATHERINE GRANGER
We have a variety of outcome tools. The main outcome is objectively looking at the physical activity levels and we're actually using a little device called a KinetaMap device which has been modified by one of our researchers, Ross Clark, and it incorporates a GPS device or it can track exactly where people walk, in particular
looking at do they do exercise outdoors or indoors and also has an accelerometer in it which measures the steps taken per day and the distance walked. So that will give us a really good idea of objectively how much activity people are doing. But we also have some questionnaires which ask an individual to recall how much activity they've done over the last week and we're interested to see how they correlate. Because in previous research in other populations, questionnaires do have their limitations and people sometimes don't report physical activity as accurately, particularly if they have problems with their memory or they're concerned about how much activity they imagine you want them to do. So it will be really good to be able to look objectively and subjectively at that measure of activity levels.

DYANI LEWIS
Now presumably a large number of the lung cancer patients will be either smokers or ex-smokers. So is this a group of people that are potentially not the most exercise-conscious people around?

CATHERINE GRANGER
It may be and that's one of the big things that happens in lung cancer, is everyone's quite concerned because they've been smokers. In fact a lot of the population with lung cancer have been smokers, but there are certainly a group of patients with lung cancer who have never smoked and that's become more and more evident now. It may be that this group of patients may have not exercised and we know that there's a link between sedentary activity and potentially a cancer diagnosis, we don't know it's a cause, but there's certainly a link. But we are really trying to investigate at the moment what exercise levels are like and physical activity levels are like at baseline, at time of diagnosis. So we don't really know that information at the moment for lung cancer; it will be interesting to find out from this research.

DYANI LEWIS
So when it comes to determining whether exercise is beneficial in lung cancer patients, what sort of outcomes will you be looking for?

CATHERINE GRANGER
That will be our next phase of research once we've finished this project, is to implement an exercise program and education regarding physical activity and to see the benefits. I imagine looking back at other types of research in other cancer populations and also looking at the evidence of exercise for other chronic diseases such as COPD which is chronic obstructive pulmonary disease, I imagine exercise will have benefits such as improving fitness levels, function and also quality of life. Another big factor for lung cancer which we hope exercise will be able to address is levels of depression, because we know that this group of patients have very high levels of depression compared to other types of cancer and other types of diseases, so it would be fantastic if we did find a correlation between improved activity levels or implementing exercise and improving depression in this group of patients.

DYANI LEWIS
With quality of life, what exactly are you talking about there?
CATHERINE GRANGER
Quality of life has many domains. We're in particular looking at health related quality of life. The questionnaire that we use with patients ask things like how do you perceive your general health at the moment, do you have trouble doing activities such as walking up and down stairs, does your health impact on your family activities or your social life.

DYANI LEWIS
Now this study is a descriptive study, so participants aren't necessarily I guess getting anything out of it as such, for example, as they might be if you were trialling an intervention of particular exercise regime. So has it been difficult attracting participants to the study?

CATHERINE GRANGER
It actually hasn't been difficult at all. I've been very surprised. The time that we're trying to recruit patients is when they've just been told they have lung cancer and sometimes it's within days or a week or two, because we need to recruit them and do testing before they start treatment, which happens very quickly as I'm sure you'd imagine. So I would have imagined it would be very hard to consent people and people would be quite reluctant, but it's been quite the opposite response. People are willing to give up their time for research, but not getting a lot of out of it in the short term. It will be people in the next five or 10 years which will benefit from this research.

DYANI LEWIS
So finally Catherine, could you give us a summary of how you think that this research might change the way in which lung cancer patients are treated in the future?

CATHERINE GRANGER
Our research team, which is here at the Melbourne University, led by my primary supervisor, Associate Professor Linda Denehy at the school of physiotherapy and also Professor Christine McDonald from Austin Health and the research, at the moment, we hope will help us understand how much physical activity people with lung cancer are doing when they're diagnosed with cancer and also during treatment and how that interrelates with other factors which impact on their treatment and their lives, such as their strength and fitness and quality of life. The results of this will then enable us to design an exercise program exactly to the needs of people with lung cancer, which obviously will need to be tested through research. But I hope that we can change standard care for people with lung cancer because at the moment exercise is not part of standard medical care for people with lung cancer, despite the fact it is for many other diseases. I hope through our research program we may be able to change what is standard care for people with lung cancer. So it's part of normal care to be provided with education or an exercise program regarding physical activity during the disease.

DYANI LEWIS
Fantastic, well thanks for telling us about your research and all the best for the rest of your PhD Catherine.

CATHERINE GRANGER
Thank you very much.

DYANI LEWIS
Catherine Granger is a physiotherapist and PhD student at the department of physiotherapy here at the University of Melbourne. You're listening to Up Close, coming to you from the University of Melbourne, Australia. I'm Dyani Lewis. For some, the prospect of exercise is probably too painful to even contemplate simple movements, let alone more strenuous activity, is sadly out of the question for many who suffer from arthritis. Our second guest on Up Close today is Tommy Liu who is based at the Walter and Eliza Hall Institute for Medical Research. Tommy's PhD research is trying to unpick some of the basics of arthritis and to do this, he is turning not to arthritis sufferers, but to mice. Welcome to Up Close Tommy.

TOMMY LIU
Thanks for having me.

DYANI LEWIS
Now there are many different types of arthritis, but could you go through briefly some of the more common ones and what causes them?

TOMMY LIU
Yes, sure. There are many different types of medical disorders that affect the joints. Three of the most common are osteoarthritis, rheumatoid arthritis and gout. Now all three share some common symptoms such as pain, swelling and stiffness of the joints, in the most cases will progress towards destruction of the joint architecture. Now just to go into each of these a little bit more, rheumatoid arthritis is considered a chronic inflammatory disease in that there is a constant and maintained inflammation within the joint. The causes of rheumatoid arthritis is not well understood, however as an autoimmune disease where our body's immune system attacks itself, we do know that there are genetic factors involved and that the main cellular players are B and T white blood cells and that the main cell signalling protein that drives the inflammation is called TNF. Osteoarthritis is considered a degenerative disease in that there is very minimal inflammation. However there is a progressive destruction of the joint nonetheless. Genetically, recent research has showed that there is a huge influence of genetics, up to 50 per cent, to a person's susceptibility of developing osteoarthritis. However in saying that, there is also physical factors involved; mechanical injury from sports, of being overweight and again normal wear and tear of ageing does contribute to development of osteoarthritis. However in saying that, ageing is related to but is not a direct cause of osteoarthritis, contrary to what some people may think. Finally, cracking your knuckles is not a cause of osteoarthritis. And finally gout is arguably the most painful form of arthritis, so gout is caused by high uric acid levels in the bloodstream. We get high uric acid levels from eating high purine-rich foods such as red meat and seafood. Now purine is a
compound contained in those foods that our body normally breaks down into uric acid, so high build up of uric acid in the bloodstream can lead to crystallisation of this compound and can lead to deposits of microscopic needles in the joints, which can induce an immune reaction. There are genetic factors involved in developing gout, however diet is the main cause.

DYANI LEWIS
So it seems that there are some quite different processing going on in each of those conditions, yet inflammation is central to a lot of them. Can you tell us a little bit more about inflammation?

TOMMY LIU
Sure. In the normal healthy joint the cartilage which lines the connecting ends of bones is smooth. The space in between the cartilage which we call the synovium is clear and the synovial lining, which are the tissues that hold the joint together, is thin and free of infiltrating cells. In an inflamed joint, the resident cells in the synovial lining become hyperactivated and start producing inflammatory cell signalling proteins that further activate other resident cells. These bring in immune cells from the bloodstream as a normal mechanism of defence for the body. The brought-in cells, white blood cells, then activate each other and induces the production of enzymes that can lead to the degradation of the cartilage lining the bones. What this will progressively lead towards is the erosion of cartilage and leading to situations where bone is literally grinding against bone.

DYANI LEWIS
So Tommy the particular protein that you were looking at is a protein called SOCS3. So could you tell me a little bit about what SOCS3’s role is in inflammation?

TOMMY LIU
Yes. Inflammation is a very potent and destructive mechanism our body uses to defend against infections. So in most cases inflammation needs to be tightly regulated. Most cells that produce inflammatory cell signalling proteins also produce a negative regulator right afterwards. A negative regulator acts as a break for the immune system, where they can dampen down inflammation and eventually turn it off. SOCS3 is one such negative regulator. It specifically controls the interleukin-6 family of inflammation.

DYANI LEWIS
So it’s predominantly produced by white blood cells?

TOMMY LIU
That is our current understanding and that is directly related to my research.

DYANI LEWIS
So tell us about your research. You are using mice in your research, so how are these mice genetically different from ordinary lab mice?
TOMMY LIU
So my research is concentrated on the cartilage, contrary to what a lot of other research is focused on, which is the white blood cells. Compared to other connective tissues around the body, cartilage only has one cell type and that's called a chondrocyte. We know chondrocytes are pivotal to joint health and that they produce proteins that maintain cartilage health and also, in this regulation, they have the capacity to remodel cartilage. However, during joint inflammation, it is commonly believed that chondrocytes are just bystanders and that other cells are actively contributing to joint inflammation. However we believe that they can initiate and maintain inflammation. So we are focused on looking at SOCS3 and chondrocytes and our hypothesis is that by removing SOCS3, this inflammatory break, that we would be able to turn the inflammatory responses of chondrocytes into overdrive and therefore amplify their inflammatory roles and highlight their contribution to disease. So we were able to develop mice that had SOCS3 specifically removed from chondrocytes and that they were unable to produce this inflammatory break and as a result, we would be able to have a look at their role in the disease.

DYANI LEWIS
What do you see when you compare the joints of these mice to the joints of normal mice?

TOMMY LIU
In our SOCS3 conditional knockout mice, which I'll just call SOCS3 knockout mice, under baseline conditions they're completely normal. However when we induce models of rheumatoid arthritis, these mice developed more severe inflammatory arthritis.

DYANI LEWIS
How do you go about developing that model of rheumatoid arthritis? What are you doing with those mice?

TOMMY LIU
So we would directly inject cell singling proteins that are commonly found in the joints of the rheumatoid arthritic patients into the knees of these mice. We would mimic what's happening in the human knee during disease. As I've said, we found more severe inflammatory arthritis, more specifically we found that there's more inflammation, more cartilage damage and more recruitment of white blood cells. When we took the chondrocytes directly from the knees, from our SOCS3 knockout mice, we found that they produced the specific proteins that can drive inflammation, they can produce the enzymes that can degrade cartilage and that they can produce the chemical attractants that can recruit immune cells from the bloodstream which fitted really nicely with our mice experiments. So altogether, this really does show that chondrocytes are active participants in joint inflammation.

DYANI LEWIS
Not just bystanders after all then.
TOMMY LIU
No, they're not.

DYANI LEWIS
So could this actually lead to new treatments for arthritis?

TOMMY LIU
It's cliché to say that it will lead to new treatments, however in the communities of cartilage biology and in arthritis research, I hope that my research will lead to new understanding of the contributions of chondrocytes to joint inflammation, to further our understanding of which signalling molecules make these cells respond and become activated and possibly open up new fields of research into how we can manipulate chondrocytes to dampen down their role in inflammation and improve cartilage health.

DYANI LEWIS
Fantastic, well thank you for telling us about your research Tommy.

TOMMY LIU
Thanks for having me.

DYANI LEWIS
Tommy Liu is conducting his research into arthritis and cartilage at the Walter and Eliza Hall Institute of Medical Research, here in Melbourne, Australia. Relevant links, a full transcript and more info on this episode can be found at our website at upclose.unimelb.edu.au. Up Close is a production of the University of Melbourne, Australia. This episode was recorded on 8 December 2011. Our producers for this episode were Kelvin Param and Eric van Bemmel, audio engineering by Gavin Nebauer. Up Close is created by Eric van Bemmel and Kelvin Param. I'm Dyani Lewis, until next time, goodbye.

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