The Cancer Professionals Podcast

Gut health and cancer care

Episode transcript

(Intro music)

Liv (00:10)

What is the gut microbiome and why does it matter so much in cancer treatments?

Emma Nicholson (00:14)

what antibiotics do essentially is that they can wipe out the healthy gut bacteria and you can get just a sort of population of bacteria that's very narrow that might be kind of restricted to just a smaller number of bacteria rather than a very diverse healthy bacteria. And that very restricted microbiome can impact their cancer therapy. So in the setting of stem cell transplant patients who've had prior antibiotics, there's very good evidence actually that that can decrease the long-term survival if they've got a very restricted microbiome at baseline.

Liv (00:46)

Hello, I'm Liv and my pronouns are she, her.

Paul (00:48)

And I'm Paul and I go by he, him. Welcome to the Cancer Professionals Podcast, a podcast from Macmillan. In this series, we chat to a wide range of guests, including health and social care professionals to lift the lid on current issues faced by the cancer workforce.

This episode is in collaboration with UKONS, the UK Oncology Nursing Society.

Liv (01:08)

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Paul (01:25)

This episode contains conversations about cancer which you may find upsetting or triggering. Listener discretion is advised.

Liv (01:33)

Hello and welcome to the Cancer Professionals Podcast. Today we're taking a closer look at the gut microbiome. We're delighted to be joined by two brilliant guests, Professor Julian Marchesi and Dr. Emma Nicholson. Together we'll explore what shapes the gut microbiome and why this area is becoming increasingly important in cancer care. So thank you so much, Julian and Emma, for joining us today. Can I start by asking you to yourselves, please? And Julian, I'll start with you.

Julian Marchesi (02:00)

Hi, my name is Julian Marchesi. I work at Imperial College London I'm what's called a fundamental or basic scientist. I'm a microbiologist by training. I'm not a clinician and I've just had interest in working in the area of the human microbiome for about the last 25 years.

Liv (02:16)

Thank you so much, and Emma?

Emma Nicholson (02:18)

So I'm Emma Nicholson, I'm a haematology consultant at the Royal Marsden and I specialise in stem cell transplantation and cell therapy and acute lymphoblastic leukaemia. And I've developed an interest in the gut microbiome. Our patients get a lot of complications affecting their gut and that is definitely influenced by the gut microbiome. So that's kind of led me to get an interest in this area

Liv (02:40)

Thank you so much. it's such an interesting topic. I suppose, particularly at the moment, we seem to hear a lot about gut health on social media and places like that, And Julian, for anyone who might be new to the topic, how would you describe the gut microbiome and what role does it play in the body?

Julian Marchesi (02:56)

So the gut microbiome has been around since we've had guts, but it's only like in the last 25 years that we started to really look at it with any interest. And initially what we used to think was the bacteria and the viruses that live in the gut, generally they're bad for you or if they get out, they cause a problem. But what we started to realise using some new tools is that actually they're like a virtual organ. They actually do a lot of really helpful jobs that allow you to function properly.

So we've started to understand that they're there and they can stop germs and bacteria and viruses coming into your gut and causing diseases. They sit between you and your diet, whatever you eat, they see as well when it gets down into the small and large intestine and they'll eat that as well. And in doing so, they make other chemicals that are really important for you to function. They also play a really, really important role in talking to your immune system.

One thing that we're really interested in understanding a little bit more about. So all this collection of microbes that live in your gut, which we call the microbiome, the gut microbiome, how they interact with your immune system, how they help you to maintain a healthy lifestyle. And sometimes when they do go wrong, what can they do to actually promote disease and how we can stop that. And very interestingly, a lot of the drugs that you take interact with your microbiome and sometimes a side effect you see and whether the drug works or doesn't work it's all down to what type of microbes the collection you have in your gut. So this is a new frontier for us. It's only been sort of opened up in the last 25 years but what we're doing is we're chipping away at it and just trying to understand its role. What does it do? It's a bit like, you know, suddenly push the liver aside and found a whole new organ there. We're in that sort of new frontier, a whole new collection of things that these bacteria do, functions that they bring to you and so we're just interested to start off with understanding what they do and when they do change is that good or bad.

Liv (04:57)

It's so so integral to our health then in so many ways. That's so interesting. And is the microbiome formed and what is it made up of?

Julian Marchesi (05:00)

Yeah. Yeah, so we now think that you're born sterile. So when you come out of the womb, you start getting exposed to the first microbes and bacteria you see will be from the mum. From the vaginal tract, if it's a vaginal birth, and from the skin, if it's a caesarean section. And inevitably when a mother does give birth, a little bit of poo comes out and the baby will be coming to contact with that. There's nothing wrong with that. It's very natural, baby will start getting some poo bacteria there. So this is the first minutes of life, is the first time the baby see the microbes and these are some viruses, not bad viruses. A lot of the viruses that we see in the gut are viruses that actually prey on bacteria. They're called bacterial viruses and sometimes we call them bacteriophage. And so this is a term that was coined many years ago to describe viruses that only kill bacteria.

Over the first five to six years of life, your microbes in your gut consolidate, they sort of establish themselves, and what dictates that is antibiotics that you have and what foods you're weaned onto. So off breast milk or formula onto solids, and then by about five and six, you have a collection of bacteria in your gut that you carry with you all the way through life. Unless you have lots of antibiotics or dramatic surgery of your gut, it's more of a stable collection.

Liv (06:27)

That's so interesting, And if I bring us on to cancer, what is the link between our gut microbiome and cancer? Is there kind of a link between cancer risk and treatments? Mm-hmm. Mm-hmm.

Julian Marchesi (06:36)

Yeah, that's a good question. There's a very strong link both in terms of stopping cancer and also sometimes promoting cancer to happen. So on the stopping side, one of the things that the gut microbes do is take components of your diet that you can't use and that's usually plant material, fibre. You we all know we should be getting more fibre in our diet, but the components of your diet which are fibre that you don't use, so they pass through your small intestine into your large intestine, the bacteria are really good at breaking that down, turn it into chemicals that then some of those chemicals can actually be protective and stop things like colorectal cancer from forming. So that's the protective side. They can do that when they're given enough fibre. The other thing that they can also make are chemicals that can cause cancer. often call them carcinogens. And so in your diet, you will have chemicals that the bacteria can modify and change and they can then cause damage to DNA that can then lead to cancer initiation and formation. So it's a double-aged sword, know, it's two sides of the same coin. They can protect you against cancer forming but sometimes they can also cause cancer.

Liv (07:43)

Thank you.

Paul (07:44)

Emma, if I could bring you into the conversation, for people who don't work in this area, how does the work you do impact in the gut microbiome?

Emma Nicholson (07:56)

So yeah, the gut microbiome is hugely impactful for our patients. patients who being treated for blood cancers, these are often very intensive treatments our patients are very immunocompromised so they're really, really high risk of infections. And as a result, throughout their cancer therapy, which may go on for months, sometimes even years, they can be exposed to multiple rounds of what are called broad spectrum Antibiotics will fight a huge range of infections, but also has an impact on the bacteria within their gut. And you can really affect the bacteria within the gut by exposure to broad spectrum antibiotics. And there is increasing evidence that that can then impact the treatments that those patients are going through. So in the setting of stem cell transplant, for example, there is really good evidence now that patients who have got a very kind of restricted microbiome. what antibiotics do essentially is that they can wipe out the healthy gut bacteria and you can get just a sort of population of bacteria that's very narrow that might be kind of restricted to just a smaller number of bacteria rather than a very diverse healthy bacteria.

And that very restricted microbiome can impact their cancer therapy. So in the setting of stem cell transplant patients who've had prior antibiotics, there's very good evidence actually that that can decrease the long-term survival if they've got a very restricted microbiome at baseline.

These patients are at much higher risk of complications post stem cell transplant. They're at very high risk of a complication called graft versus host disease.

We do know that the baseline microbiome of patients going through very intense cancer treatments, such as stem cell transplant, can hugely impact on their outcome and can massively increase the toxicity of that therapy, which ~ is something that's obviously a huge area of concern to us if we're going to be increasing the risk of complications post-transplant.

Paul (09:54)

And for anyone sort of hearing that term about stem cell transplants what do you actually mean?

Emma Nicholson (10:01)

So stem cell transplant is used for very high risk blood cancers that either don't respond or have got very high risk baseline genetics that would put them at high risk of relapse. And so it's not used in all cancer therapies, but it's for very high risk haematological malignancies where we feel there's a high risk of relapse.

And there's two types of transplant essentially. There's one where you're using a patient's own stem cells, but there's also a type of stem cell transplant where you're using a donor, so a genetically matched donor that's another person that's donating their stem cells. And what we're relying on is we're using the immune system from another person in that setting to fight against their cancer long term. So although we're using cells that are a genetic match, there is a difference between the donor and the patient and that itself can help prevent relapse of their cancer long term. So we're using the immune system from another person basically to fight against their cancer long term.

Paul (10:59)

And in terms of I suppose, prehab for the gut and for the microbiome, and the immune system, for anyone new to this area, you explain a little bit more about that?

Emma Nicholson (11:11)

As we said, there's evidence that if you've got a non-diverse gut microbiome prior to transplant, then you can have more complications post-transplant, more of a complication called graft-versus-host disease. And so there are studies ongoing to see, you pre-habilitate the gut? Can you use donor faeces essentially to transplant into a patient's gut to essentially rehabilitate their gut with healthy gut bacteria. So you're going to try and repopulate their gut with a more diverse microbiome essentially. And there are a number of studies looking at that to see whether you can use that to improve the gut microbiome and reduce the risk of side effects post stem cell and the team at Imperial have a study that has been recruiting in the UK is now close to recruitment called the MAST study where patients prior to this allogeneic stem cell transplant are given a transplant of fecal material called an FMT and that's given before the transplant to see if that can reduce the risk of complications post transplant.

And so that's a big area of interest is can you repopulate their kind of non-diverse gut microbiome with a healthy donor gut microbiome and in the long term can that reduce the risk

of complications? And so that's a big area of interest is can you manipulate the gut microbiome to try to reduce the risk of side effects post transplant?

Paul (12:35)

And is that a good point to kind of bring in Julian and to just maybe tell us a little bit more about that?

Julian Marchesi (12:42)

Yeah, so it's not something that we just made up down the pub one day and thought this is a great idea. Let's go and find a stool sample from an individual and pop it into another person.

Historically, there was a recording ~ in China in 4 BC of yellow soup, which was sieved stool slurry being used to treat gastrointestinal problems. And then in the 1950s, a gastroenterologist in America realized that you could treat an infection of the gut called C. difficile infection with a stool transplant. And then we sort of forgot about it. And then the C. difficile infection story popped up again. And what we started to realize was, as Emma was saying things like C. difficile infection of the gut are caused because we wipe out the good bacteria in the gut that protect us against this bacterium getting in. And we wipe it out using antibiotics. And so while antibiotics are great for treating infections, they also have collateral damage. And so as as scientists and clinicians we were looking to see, well, what are the tools are available to us to reset the gut and the gut microbiome?

You can try diet. But that's hit and miss and not many people stick to diet and we haven't really developed the tools very well. But we thought, look, in the C-difficile infection setting, which is where an individual gets this really nasty infection of the gut because what we've done is we've wiped out the bacteria that protect the gut against this other pathogen, this bacterium getting in, what we can do is we can reintroduce a healthy gut microbiota literally by putting a stool sample into their gut.

And so that worked brilliantly. And on the back of that, a whole load of different studies popped up. And one of the studies that caught our eye was the fact that in some cancer patients who don't respond to these new immune-based drugs, these immunotherapies, there was a group in America and a group in Paris that showed that if you manipulated their gut microbiota of somebody who doesn't respond to these drugs, these immune-based drugs, you can turn them back into a responder.

And so this was giving us a clue that A, if you do have low diversity depleted bacteria in your gut and you put in a very rich diversity new gut microbiota or microbiome, you can reverse that non-response to a drug, which was telling us that there's some communication between the gut bacteria and the immune system. Now we didn't know what it was, but we had a cause and effect. So we weren't too worried at the moment, and we will always get to that mechanism, but we had a strong cause and effect. You took a stool sample from a healthy individual, put into somebody who's not responding to an immune-based treatment for cancer, and you can turn

them into a responder. And we were saying, and as Emma was saying, the evidence was also building that in immune-based interventions, whether it's bone marrow stem cell transplant, whether it's these immune-based drugs, that if you do have a low diversity of gut microbiota and you make it into high diversity, then there's benefits for the host. So what we initiated was this study where we took stool donors and again they're not just random people we find on the street, these people are really really well screened. They're screened for a whole range of blood, and bacteria, then viruses, pathogens, We do a ~ lifestyle questionnaire. So it's really in depth, much more in depth than you would have if you were going just to give blood to make sure that you're healthy and your stool sample is clear of any known pathogens that we can think of that we don't want to, especially to transfer to any of Emma's

So the donor screening is quite involved. And especially with Emma's patients being immunocompromised or immunosuppressed, we don't want to transfer anything that could give them an infection. So the whole idea is as Emma was saying, we pre-habilitate. It's no good trying to change the gut microbiome after they've started their cancer treatment. We want to get them into a better place before they start. And the idea is, it's a bit like what they do in surgery, where they try to get patients a little bit fitter before they go in for their surgery. They pre-habilitate rather than rehabilitate after. And we're doing the same. We're treating the gut like an organ and we're trying to get into a better position. So when they turn up at Emma's clinic,

Hopefully, they'll be in a better position to receive the medicine and actually respond better to it.

(Ad)

Liv (17:12)

This conversation really highlights how important nutrition is, not only because of its impact on the gut microbiome, but also because we know that malnutrition can negatively affect how people with cancer respond to treatments.

Paul (17:24)

Yeah that's right, Liv and if you support people living with cancer, you'll know just how complex nutrition can be.

Liv (17:30)

Macmillan's Enhanced Acute Oncology Nutrition e-learning module explores nutrition in the context of acute

Paul (17:37)

You'll learn what malnutrition is and how it can develop. Why acute symptoms can impact nutritional intake and explore key interventions used in acute oncology practice.

Liv (17:46)

That sounds great. If you'd like to find out more, head to the episode description. Now let's get back to the conversation.

Emma Nicholson (17:53)

In terms of recruiting patients to this type of trial, it involves quite careful discussion and also lot of careful communication around it because it is the concept that you're going to be asked to swallow a capsule of someone else's faeces. is a lot of patients when you have that discussion with them.

Their immediate response is absolutely not. But then I think if you take the time to go through it and Julian and his team developed these amazing kind of patient videos as well, just talking them through the process. I think you kind of have to have the discussion about actually what those potential benefits are in going onto a study like this as well. And definitely we had a number of patients who were very happy to go on to the study and and also just so they can be talked through actually what's it going to feel like to take these capsules, is it going to smell, Yeah, so there's a lot of kind of anxiety around that and I'm sure that's something that this study also will be collecting data about. But there's various ways of delivering FMT as well, so probably the one that is most palatable is going to be a capsule that you can swallow, but there are other studies that are using FMT where they're given by a kind of a rectal catheter or in the old days these used to be given by a kind of slurry of a nasogastric tube. So it's kind of the technology sort of moving on pretty quickly. So hopefully it becomes much more, a much more standardized product, a kind of off the shelf product. And as Julian was saying, these are kind of carefully screened, manufactured in really good manufacturing kind of procedure. It's very tightly regulated and has to be, I think if this is going to become a therapy.

Julian Marchesi (19:36)

Like I said, we actually make them to the same standard you make a drug.

It's obviously not sterile because it's a stool we do make it to the same sort of level as a drug. So we are licensed or we will be licensed. And the people who make this are licensed as if they were making any drug in the UK. The MHRA are coming in. They will assess us. They will test us. And so it's not like, let's go into the lab and make something and throw some into a jar. It is very stringent. And also, I'd add it's really, really safe. you know, thousands and thousands of these done around the world for a whole wide range of different disease and indications and we've put them into patients who've had kidney transplants so you know solid organ transplants who are pretty sick at times because they're immunosuppressed to make sure they don't reject it.

We've had very few if any side effects and the side effects are just a little bit of burping, it'll be feeling sometimes a little bit nauseous, maybe a bit of flatulence but nothing more than that and so you know to say that it is safe it's mostly a lot of time safer than a lot of maybe some of the medicines that Emma uses in treating the patients, you know. In fact, in our MAST study, when we were recording the safety profile, we usually stopped recording when they started the

treatments that Emma would look at because a lot of those have worse side effects than what we were giving.

Emma Nicholson (20:57)

And that's, think, really key. The other kind of aspect of FMT in the setting of stem cell transplant is that it's also being trialled for treatment of a complication of transplant called graft-versus-host disease, which is where the immune system from the donor is attacking healthy parts of the patient's body, which is a kind of side effect of the therapy. And in particular, you can get a very severe form of graft-versus-host disease where you get inflammation of the lining of the bowel and these patients can have very high volume diarrhoea, essentially intestinal failure where they're kind of malabsorbing and just having continuous diarrhoea. So, and that's a really challenging complication to treat and we have to treat it with really, really high doses of immune suppression, which has got a whole host of side effects. So FMT is now being used in the setting of very severe graft-versus-host disease of the gut to treat this inflammatory condition of the gut.

It's being used in patients who've failed kind of multiple lines of immune suppression, but also the benefit of this, and it's been shown to actually have very good response rates in very high risk patients, the massive benefit of a treatment like this is the side effect profile is so low essentially, and that is if you can develop a treatment for a potentially life-threatening complications that doesn't have its own treatment-related complications, I think that's a real kind of goal of a therapy like this.

Liv (22:19)

That is amazing. That is so, so exciting to hear about as well. And like you say, about not having those complications for the impact for patients then is, yeah, unbelievable. Just in terms of kind of the the evidence from the trial. when is the timeline on this?

Julian Marchesi (22:34)

So as Emma mentioned, the MAST study has just finished recruiting December last year, and we have a year follow-up then on those patients who we finally recruited in December.

After that we'll do the data analysis and the number crunching and come out with an idea of whether or not we have modified the gut microbiota. So the primary outcome for the study was not to see if we've improved treatment. We weren't powered to do that. We had 50 individuals in each arm, no, 50 individuals in total in fact, and so it's individuals taking a faecal microbiota transplant, an FMT, in a capsule form and 25 were having a placebo which was just a sugar capsule effectively. But what we wanted to know is could we in this cohort A, modify and show that we're changing pre-habilitating the gut bacteria, making it more diverse, making it a richer community in the gut compared to the placebo and then some of the secondary ones we were looking at, know, and did they get any bloodstream infections, safety profiles, etc. etc. So that then will kick us on to a phase three trial. So that was what we call a phase two trial. So the phase three trial would then be rolling it out into a much larger population, maybe three to four hundred patients across the whole of the UK and determining things like survival, response to the

medicines and whether they get that graft versus host disease and if we're reducing it in that arm who are having the faecal microbiota transplant.

Emma Nicholson (24:02)

Another type of therapy which is also of interest to me is something called CAR T-cell therapy which is where we're, it's again a treatment for a number of high risk blood cancers where we take cells from the patient's own immune system and they get genetically modified with a gene that then leads to those cells expressing a receptor so that when they're given back to patients at a later time they can more effectively target their blood cancer essentially and that's a treatment that's been around in the UK now for kind of seven plus years. It's kind of standard in our treatment, but there are patients that either don't respond to CAR T-cell therapy or either relapse after initial response and it has got potential side effects. So there's increasing data that the gut microbiome also impacts your response to CAR T-cell therapy and your long-term survival.

So we're also interested in looking at the gut microbiome in the setting of CAR T -cell therapy. And we're hoping to do, and in a similar way to Julian and his team at Imperial, we're wanting to work with them on a study in the setting of CAR T and whether you can modulate the microbiome in the same way as has been done for stem cell transplants. So these are kind of other areas of interest in blood cancers and also in a setting of solid tumour immunotherapies and trying to modulate the microbiome pre immunotherapies.

Liv (25:23)

That's great to hear that it has so many applications as well. It's brilliant. So thinking obviously about this is still very much in trial and not something that's available very widely at the moment. So for kind of health and care professionals who are supporting people with cancer now, obviously diet comes up in a lot of conversations about is there anything people should be restricting or certain things that people should be eating before and during treatments? What would your advice be to professionals when they're asked that question? How should they be responding? What kind of advice should they be giving?

Emma Nicholson (25:55)

So, yeah, so this is a question that comes up a lot and there used to be, and there still is probably practice in some cancer centres around the world, there used to be a real restriction to patients' diets when they were going through treatment for blood cancers because they have very low white cells, very low immune systems who are potentially high risk of infection. So there used to be a recommendation that you really restrict patients' diets and it's kind of termed sort of either low bacteria diet or neutropenic diet and that would be kind of stopping patients from eating fresh fruit and vegetables, making sure everything's very very well cooked, not eating anything raw and so patients would end up having a really restricted diet of quite bland maybe kind of packaged foods and so you're restricting kind of actually a lot of very healthy foods, high fibre foods.

So the evidence base actually that you need to have that neutropenic diet now is actually not strong at all and it's very controversial and there's probably increasing evidence from quite big analysis that actually the converse is true is that you actually might be doing harm to them by giving them a really restricted diet because they're not having enough fibre and kind of fermented foods and kind of healthy kind of vegetables and fruits. So that kind of very non restricted kind of diet actually might be harmful to the gut microbiome. So that is kind of, we certainly in our centre do not recommend a neutropenic diet anymore. And our dietitians, we've, will be kind of talking to patients throughout their kind of cancer therapy and giving them recommendations about what they should be eating so it's trying to not sort of scare patients that they need to actually eradicate stuff from their diet. And we just want them to eat healthfully and eat as much as they can.

Definitely nutrition going into a high intensity treatment like a stem cell transplant is really key. And again, this whole prehabilitation of whether you can prehabilitate patients prior to transplant with diet and also better nutrition, also exercises, they're all kind of critical things in their recovery post a really high intensity treatment. So yeah, so diet I think is a real kind of area that is probably under researched in terms of what we should be recommending, but.

Yeah, that kind of older way of restricting the diet we've moved away from definitely.

Liv (28:10)

Mm-hmm, thank you. And Julian, is there anything you'd like to add to that?

Julian Marchesi (28:14)

No, I mean, I'm not a dietitian, so I don't want to give advice and I'm definitely not an oncologist, but the fibre story is a story that we do need to address because even in just the population, 90 % of people don't get sufficient fibre in their diet every day. And there are studies which show that if you restrict fibre or you take people on high fibre and put them on low fibre and you do a sort of crossover study where you give the low fibre people high fibre, you can definitely measure markers of cancer progression in the gut. So the people on the high fibre go into low fibre, start producing more markers of cancer initiation and the people on low-fibre going to high-fibre have a reduction of these markers and so we know the fibre is protective against cancer starting in the gut. doesn't say you're not going to get it but it's just like anything it reduces the risk and so as Emma was saying for just in the general information so for people going in to treatment I think you want their gut microbiota in the healthy position that you can and you treat it like an organ.

Liv (29:08)

Mm.

Julian Marchesi (29:18)

You know, if you want to look after your lungs, you don't smoke. If you want to look after your liver, you don't drink copious quantities of alcohol. If you want to look after your heart, you do some exercise. Well, with the gut, the story is you give it fibre. That's what it really thrives off. And then in doing so, it produces a whole range of chemicals that can talk to the immune system, talk to your cells in your gut and keep them healthy. And that's what you need to promote. But you need to promote that at a young age. You know, when you get to my age,

it may be bit too late, but when you're in your 20s, that's when you should be really, really investing in your gut. you know, there is a story developing and Emma will know this about young people getting colorectal cancer, which used to be a disease in your 60s. But we're seeing more younger people getting it. And some of the talk is, is it all around ultra processed foods? I'm not going to say anything more than that, but ultra processed foods generally are not generally high in fibre. But you've got to be careful ultra-processed also include wholemeal bread, is high in fibre, you know, so, but generally a lot of ultra-processed foods do not contain high levels of fibre and we're talking about more than six grams in every hundred grams of the product. And so yeah, if there's one thing I always tell anybody who wants to hear it, here it is, fibre max. Have a look at how much fibre you're taking in your diet.

Paul (30:39)

That's really interesting. And Emma, is there anything else you'd like to before we move on?

Emma Nicholson (30:44)

I suppose, again, in the kind of setting of stem cell transplant in terms of nutrition, for our patients that get this severe form of gut graft-versus-host disease who have really high output diarrhoea, again, nutrition in those patients is really critical. And the kind of thing that we used to advise, which we've moved away from, is that you would kind of have to completely rest the gut and stop anything going into the gut and giving patients' total parental nutrition, so just nutrition through their veins. They weren't eating, having any nutrition kind of orally. But actually, again, that is probably detrimental to their gut recovery because you need to have food and fibre going continuously into your gut so that you can help not just maintain your gut microbiome, but also maintaining the kind of health of the lining of the bowel, so the integrity of the lining of the

So again, these are kind of areas that have been the evidence base for stopping patients with gut GVHD from actually eating anything, is definitely, we're moving away from that and actually realizing we want there to be a continuous transit of food throughout the gut or feeding throughout the gut throughout their recovery, even if it's just a little bit. And it's tricky because these patients don't always tolerate a lot of oral intake because they're having a lot of diarrhoea, but it's a sort of trying to just even give what we can and also trying to introduce, as Julian said, fibre quite early to help recover that gut health and kind of trying to help them recover from their graft-versus host disease.

Julian Marchesi (32:11)

Because one of the things that you've got to remember is if you don't feed the gut bacteria, they will look for other sources of food. And a lot of that time it is things like mucin in your gut. They'll swap over to feed on whatever they can. So if you're not feeding them the nutrients they want, which are fiber and some dietary factors, they will look elsewhere. So they will start attacking the mucin layer of the gut, which is there to protect the cells underneath from the bacteria. And so we're going to have a knock on effect that you're really compromised.

In gut health and the role of the gut which is to act as a barrier between what's in the gut and what's in the host. You know, you have that one layer of cells in that gut which is a barrier between what's in the gut. And if that barrier becomes compromised then molecules and chemicals and viruses and bacteria can move across and potentially infect the host.

And so, you know, it is a balance. isn't just the gut bacteria will just stop and wash out. They'll start thinking, well, I'm not getting the food I'm used to getting. Where else can I turn to getting food? And then some organisms will die off and more detrimental organisms may bloom and blossom in the gut because you removed those fiber, the fibers that some bacteria use to stop bad bacteria from growing. It's a dynamic system. It just doesn't just wait for you to do something. It'll it'll swap. It'll change. It'll adapt.

Liv (33:25)

Mmm.

Julian Marchesi (33:31)

And if you don't give it what it's used to, then organisms that you don't want blooming in the gut do bloom and can cause other problems.

Liv (33:39)

in what kind of timeframe can that start occurring? wow.

Julian Marchesi (33:42)

24-48 hours.

There are very nice studies that have taken individuals who say were omnivores, eat anything, turn them into vegetarians and vegans and you can start measuring a signal 48 hours later when they have the stool coming out. It's a very dynamic system, it changes really quickly. That's why giving antibiotics will impact it. The minute antibiotics and oral antibiotic goes in and it gets down into the small and large intestine, it's having an impact straight away. And there was a NICE paper that came out recently that said eight years later we can still see an impact of an antibiotic you took. It was a study from a Scandinavian group looking at about 15,000 patients and looking at the historical records of antibiotic use and then taking stool samples and showing some

antibiotics one or four years later, some seven to eight years later. You can still see a signal because of that antibiotic.

Paul (34:33)

Sounds like such a fine balance.

Emma Nicholson (34:34)

Yeah, just I kind of yeah, antibiotics stewardship and overuse of antibiotics is also really critical. And as a haematologist, we use a lot of antibiotics and we definitely overuse them because we you have to in immunocompromised patients, you can't not treat infection that will lead to to death very quickly. But also we are we definitely overuse antibiotics and we and it's having better tools to say, I don't need to use antibiotics in this context or I can deescalate my antibiotics and that because we are seeing increasingly in hospitals more and more multi-drug resistant organisms. So bacteria that don't respond to the kind of toolbox of antibiotics that we have and that's a huge concern and that's partly driven by overuse of antibiotics. So it has impacts in all kind of areas. So yeah, we need better ways of trying to reduce antibiotic use wherever possible and the kind of rehabilitation of the gut with FMT Julian and his team have also used that for patients who've got multi drug resistant organisms to get rid of that colonisation. So, and that itself can potentially reduce the risk of infections, reduce the risk of hospitalisation and long term stay. So that's kind of got influence everywhere.

Julian Marchesi (35:41)

Mm.

Julian Marchesi (35:49)

It's funny, it's how we first got into this area. Haematologists from the Hammersmith Hospital came to my colleague and said to him, look, we've got a patient here who's got an antibiotic resistant bacteria in their gut, and he's got the C. difficile. And the last patient who was in this situation, we treated and died of an untreatable bloodstream infection. So they gave him the stem cell transplant, the patient before, because they were immunosuppressed, they got a bloodstream infection, but it was resistant to all the antibiotics they had. And so the patient had their bone marrow transplant, their stem cell transplant and survived. And on the back of that we did some more and then we found it was actually quite good at getting rid of these really problematic and hard to treat bacteria.

Paul (36:34)

It's a really fascinating topic and we're just going to move on to the final section of the conversation today where we ask each of our guests, what would you like our listeners to take away from today's episode? And Julian, shall I start with you?

Julian Marchesi (36:51)

I think one of the things I'd like people to take away is don't be scared of a stool transplant. It sounds disgusting and as Emma said, you do, the clinicians do explain to the patient, you can look at them thinking, you're going to do what? But it's really safe and we're finding more and more areas where it's benefiting patients. To modify the gut microbiome using a full stool transplant as a capsule is having benefit in areas we hadn't anticipated before. So it could be minimising side effects to drugs, making drugs work again, treating patients who are having chemotherapy or immune-based therapy in cancer. Watch out for it. I think it's going to blossom and I think, you know, watch out for stool transplants becoming much more mainstream.

Paul (37:40)

Thank you, and Emma.

Emma Nicholson (37:41)

Yeah, no, I think in terms of takeaway, I think it is just the importance of the gut microbiome in all that we do in terms of cancer therapy. And yeah, I think this is going to impact not just how we screen cancers, so you can use the microbiome also to predict how someone is going to respond to a cancer therapy. So I think we're to be using this much earlier as well in the patient pathway in terms of prediction models and it's also going to impact how we treat patients. You might in theory could we be looking at kind of microbiome signatures that is going to influence what treatment we give a patient. So I think this is a really interesting and fast moving field and it's really just at its infancy but I think this is going to become as Julian said much more widespread in cancer therapy.

Paul (38:31)

Thank you. Yeah, thank you, Julian and Emma I think you've helped bring a really complex and exciting topic to life in such an accessible way during our conversation today. Who would have known we end up talking about stool transplants and we're really grateful you can join us on the Cancer Professionals podcast.

Julian Marchesi (38:52)

You're welcome

Emma Nicholson (38:52)

Thank you.

Liv (38:54)

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Paul (39:15)

If you enjoyed this episode, follow us so you don't miss our next conversation. We'll be joined by Andrew Crumby, Rodney Mountain and Eleanor Ogilvie to talk about the cancer tapestry.

Liv (39:27)

We'd love for you to rate our show and share with your colleagues. Get in touch with us by emailing professionalspodcast @ macmillan.org.uk. New episodes are released on the first and third Wednesday of each month.

Paul (39:38)

I'm Paul.

Liv (39:39)

And I'm Liv and you've been listening to the Cancer Professionals Podcast by Macmillan Cancer Support.