Rheumatology Ref 168

with Robert Moots

2nd June 2021

TRANSCRIPT

Please note, this is not a verbatim transcript:

- *Some elements (repetition or time-sensitive material for example) may have been removed*
- *In some cases, related material may have been grouped out of chronological sequence.*
- *The text may have been altered slightly for clarity.*
- *Capitalisation and punctuation may be erratic…*
- *There may be errors in transcription. If something appears odd, please refer to the recording itself (and let us know, so that we can correct the text!)*

Steven Bruce
Good evening and as always a warm welcome to the Academy. It's great to have you with us. And I'm sure you're going to have a really fascinating evening CPD with us this evening. I'm pretty convinced that most of the speakers we have on this show are fairly eminent in their own way. But sometimes you just feel a little bit overawed by the CVs that you read. And tonight's no exception. I'm joined by Professor Rob Moots, who is a professor of rheumatology, but he's not any old run of the mill professor of rheumatology. Not only does he have a medical degree, he has a degree in immunology, he has a PhD from Oxford, he's lectured at Harvard, he's been a keynote speaker on every continent on the planet apart from Antarctica, sadly, he's written over 200 articles for the prestigious medical journals, again, none of the run of the mill stuff. And he's actually been the editor in chief of the journal Rheumatology. Give him 5 million pounds of research money and he and a small team will find out what neutrophils have to do with rheumatoid arthritis. And I suspect we'll hear a bit more about that later on. And his Centre of Rheumatology in Liverpool is a European Centre of Excellence. Add into that in his spare time he climbs Kilimanjaro and Everest. Rob, it's great to have you with us. I'm glad you've got some spare time to spend on it.

Robert Moots
Well, thank you very much, Steven. It's really good to be here tonight. Thanks for inviting me. I'm looking forward to a really fun evening.

Steven Bruce
Well, I hope so too. We were talking, I was mentioning just a moment ago that you've done a lot of work on neutrophils and RA. And I wonder if we could start with that because it sounds interesting. It has implications for testing for RA, I gather.

Robert Moots
So it's kind of funny, really, in my scientific training, I was interested in a certain type of white blood cell called a lymphocyte. And I used to throw away these contaminating cells and neutrophils. But of course, neutrophils are the most abundant cell in the human body in the immune system, the most abundant white cell. And when I moved to Liverpool, I learned I was doing a really crazy thing, I was throwing away the really important cell that we have been studying ever since. So that's kind of transformed our biomedical basic science research where we've reoriented things from one white cell to another white cell. And trust me, there's a very big difference between the two.

Steven Bruce
Does it have implications for our understanding of the white cells themselves? Because normally don't we associate neutrophils with bacterial infection?

Robert Moots
Absolutely, we have. We're here today enjoying this broadcast because we're alive and we're alive because we have functioning neutrophils. Without these white blood cells, we'd be dead of infection, and we wouldn't survive beyond the first few months. So neutrophils are crucial for life. But the problem is that they can go wrong. And we've been studying how they might go wrong to cause inflammatory problems, such as rheumatoid arthritis.

Steven Bruce
And what's the implications of what you've discovered?

Robert Moots
Well, it's been very difficult in the past to try and target neutrophils because if we think neutrophils, white blood cells are causing problems, that means that if we can identify that, we can try and selectively switch them off to stop the problem but stop us from dying of infection. So some of the work that we've been doing has done just that we've actually found a way to switch off all the bad function of neutrophils, and that's causing various forms of arthritis, but in no way affect the really crucial role, which is to protect us from infection. So that's been a very interesting breakthrough. And this is something that we're kind of looking at as time goes by, as to how that might be used in a whole variety of diseases, and also potentially COVID.

Steven Bruce
Really, in what way?

Robert Moots
Well, in COVID, one of the problems is that a few people, a small percentage of people become very ill, because they have what we call a cytokine storm. And that's kind of like mutiny in an army. It's like friendly fire. It's like nuking a whole ammunition dump, an exploding everything inside the body. So again, one of the things we found is a new medicine that we've been helping develop for osteoarthritis can also switch off some of the inflammation chemicals that can cause really bad COVID. So I'd have never thought as a rheumatologist that some of my work could have even be useful for this terrible COVID epidemic. Watch this space.

Steven Bruce
I'm not sure I've seen anything about that in the press or the general press. Has there been anything published about that?

Robert Moots
Yes, there has. There's been a couple of press releases from an article that we've published midway through last year, where a new medicine that is being developed called APA. And I can tell you more about that later. We've been testing the effects on neutrophils and as I say, we found exactly that. It can switch off neutrophils from producing the very toxic IL six and other inflammation chemicals but no effect on them killing bacteria. I think that's actually been on the front page of The Daily Express apparently.

Steven Bruce
That would explain why I haven't seen it then. We've actually had a question that came in very, very early from Amelia. It's connected to rheumatoid arthritis. Amelia says that she wonders about the significance of a positive rheumatoid factor and whether a high level would lead to RA.

Robert Moots
Well, Amelia, that's a very good question. Because in rheumatoid arthritis, we can measure things like rheumatoid factor. Rheumatoid factor is an antibody. The trouble is, though it's often positive in people

with rheumatoid arthritis, it's often also negative. So having a rheumatoid factor that's positive really doesn't help us very much. It doesn't help with the diagnosis, because healthy people can have rheumatoid factor. And Amelia if your mum has got rheumatoid arthritis there's a very big chance that you will have rheumatoid factor. But hopefully, you'll never have rheumatoid arthritis. So, diagnostically, it's not helpful. But prognostically, it can be helpful, because if people with rheumatoid arthritis have got a very high amount of this antibody, rheumatoid factor, then they're likely to do worse, or we need to target our treatments better. There is a different type of antibody, the so called anti CCP, or ACPA antibodies. And these are much more sensitive, correlating with rheumatoid arthritis. So rheumatoid factor, old news, anti CCP antibodies, more current state of the art ways for making diagnosis.

Steven Bruce
I think I read in your bio that one of the things that's come out of your research is an ability to determine which medications are going to be effective in treatment of RA. Is that the case?

Robert Moots
So that's been some very provocative results that we've been finding. What we've been doing, again, to go back to these favourite cells, the neutrophils, we take people with rheumatoid arthritis, we purify the neutrophils, we do what we call transcriptomic analysis. So that's like the next generation of genetics. So genetics measure the genes that we've got, we've got the same genes in every cell in our body. But sometimes in some cells, some genes will become activated, and in other cells, other genes will be activated. If we measure the transcriptome, we're measuring genes that will become activated. And when we look at that, in patients with rheumatoid arthritis, we find some very provocative signatures, which if you've got that type of signature, it can help predict response to some of the really expensive designer drugs, the TNF alpha inhibitors. It's still early days, but it looks very promising there.

Steven Bruce
Right, okay, and so what now then is the medication of choice or general prognosis for people with RA, because it used to be a pretty depressing disease to have, didn't it?

Robert Moots
It was an awful disease before my time, which wasn't all that long ago, rheumatoid clinics, rheumatology clinics will be full of people in wheelchairs. And it's not a surprise because we were just terrible at managing this rotten disease. We'd wait until people were almost in a wheelchair, before we actually use the drugs that are likely to work. So we waited until there was damage, then we gave effective drugs, and it's not surprising, they weren't very effective. So the way that things have revolutionised is that our job now in rheumatology is to prevent damage. So we want to use the powerful drugs, before the damage occurs and stop that happening. And that's really revolutionised the treatment, even with the older fashioned drugs such as methotrexate. If we use the older drugs better, there are better outcomes, let alone the newer generation of biologic drugs.

Steven Bruce
Right. I suppose, what I should have pointed out to everybody before we started is that when I look at the list of things that you treat, it's pretty much everything which is autoimmune or ends in -itis or -osis. So there's a whole load of stuff on the list of conditions that you cover, and I don't want us to be

constrained to rheumatoid arthritis or ankylosing spondylitis, which was actually on the holding slide this evening. What is it you treat most of? Because again, you are a clinician as well as a researcher.

Robert Moots
Yes, in fact, most of my time is actually looking after patients. And it's funny because, as an academic, your hospital wants you to do all clinical work, but your university wants you to do all research. So we have to try and balance all of that. So I'm interested in situation where there's inflammation. I'm not very good at sprained ankles. I'm not very good at a little bit of wear and tear. But I'd like to think I'm better at inflammatory problems. So that can be inflammatory arthritis, like rheumatoid arthritis, ankylosing spondylitis, it could be vasculitis, which is a really strange group of diseases with really weird names, where you can get any bit of the body going wrong. Funnily enough joints tend not to be affected. So as a rheumatologist, people always wonder why we do vasculitis and other things such as lupus, which is a very interesting inflammatory disease, causes a lot of problems and can be a real trip to treat. The one that perhaps would be the most unusual is a disease called Behcet's syndrome. Now, Behcet's syndrome is a really weird and rare disease in the UK, where again, people can get all sorts of problems, particularly ulcers in various places, eye problems can cause blindness, strokes, all of the things you don't think a rheumatologist would see. And the strange stuff, we developed a National Centre there. So there's a lot of patients we see from all around the country in different countries with this weird condition that people can't pronounce the name of, let alone understand much about.

Robert Moots
Yeah, I was interested to read about to Behcet's disease because that's just one division of vasculitis as a whole, isn't it? And I guess the thing that strikes me about this as you know, I mean, the audience this evening, we have some medical doctors in the audience, but largely it will be osteopaths, chiropractors, and physiotherapists. So, we're used to dealing with the physical signs and symptoms that people present with. But I noticed that when we look at SLE or lupus, when we look at Behcet's and things like that, quite often, they might present with things which could be masquerading as musculoskeletal problems, and so perhaps you can help us in making sure we can farm them out to the appropriate expert at the earliest juncture.

Robert Moots
So lupus is a very good example of that. Lupus is an autoimmune disease, you kind of make an autoimmune response against your own cells. And you can measure antibodies against your own DNA. That's something that can cause sore joints. It can look in many ways similar to rheumatoid arthritis. But lupus is named lupus because lupus is Latin for wolf. And one of the problems in lupus is that people can get a rash, particularly in the face, across the nose, bridge of the nose and cheeks, when they go out in the sun. And strange enough, that's where the myth of werewolves may have come from. Because people who had lupus wouldn't go out in the daytime, if they did go out in the daytime, they'd got a strange butterfly shaped rash, but if you've got a bit of a warped imagination, you might think somebody is turning into a wolf. So joint problems, skin rashes, hair dropping out in clumps, those are sort of things that make me think about possible lupus because although the joint problems look similar to rheumatoid, and people can get deformities, they don't get joints being eaten away with erosions in the way that happens in rheumatoid arthritis. So I suspect some of your group will probably have seen lupus, certainly, it's

common enough that you were likely to be seeing patients with that. And if people do have that, they can have sore joints, inflamed joints, but it tends not to damage joints.

Steven Bruce
Right. How common is the rash because it's not universal is it?

Robert Moots
It's not but it's one of the defining features of lupus in most people. It's not that you see somebody coming in looking like a werewolf. It's more like, people would say, you know, when I go out in the sun, I get a bit of a scaliness on my face, on my cheeks, it will probably be the present in more people than not. And it would be a warning signal that there's potentially some autoimmune disease. Now, I don't know about you, Steven, but if I go out in the sun, I can get a kind of a, prickly heat type rash. And I think it's very healthy to stay away from the sun. So everybody can sort of say, I might have a bit of a problem in the sunlight. But in lupus, it's very different, very striking, and very different for what any of us might get if we'd go out in the sun.

Steven Bruce
Right, so easily distinguishable, say from someone who simply gets a sort of a blush like rash. It's scaly, you said earlier on.

Robert Moots
Yes, it's scaly and it goes across the bridge of the nose. Those are the sorts of things that are red flags for that and also, many people could notice hair getting a little bit thinner. But in lupus, it tends to come out in patches and can lead bald clumps around the scalp.

Steven Bruce
Okay. You'll find Robert, I'm going to have to go back in time a bit occasionally in our conversation, because when the questions come in, they might not have caught up with with our conversation. Pippa's sent in two observations. One is that the cytokine storm was a common problem with the first SARS virus as well, but I think that's a well-established connection between both Coronaviruses who's on board. But she also asks whether GPs routinely test for anti CCP.

Robert Moots
Well, Pippa, that's a very good question because GPs would always tend to test for rheumatoid factor. And that may or may not be helpful because a lot of people with rheumatoid don't have rheumatoid factor. And a lot of healthy people do have rheumatoid factor. It's variable in different parts of the country in the UK, and in different countries, the accessibility of anti CCP antibodies in primary care. In many other countries it's very readily accessible. In the UK, the UK NHS tends to sometimes, in some areas limit it to rheumatology, which is just the way it is really. So rheumatoid factor, helpful, but don't make a diagnosis based on that. Anti CCP antibodies, if you actually detect it, it does mean something. And the funny thing with anti CCP antibodies is that you can get some healthy people walking around with lots of anti CCP antibodies but be very healthy. But in the future, they have a very high risk of developing rheumatoid arthritis. So it can be predictive.

Steven Bruce
Right. So did we actually answer the question of whether GPs are sending people for anti CCP testing?

Robert Moots
Some parts of the country do request it. It's certainly readily accessible in secondary care. But in primary care, some GPs can access it, and some can't.

Steven Bruce
Right. Jen's asked whether somebody with an autoimmune disease of another nature is predisposed to RA?

Robert Moots
Well, Jen, again, a very good question, what we tend to find is, if people have one type of autoimmune disease, they're a little bit more likely to potentially get another one. And if you have a family history of autoimmune disease, you've got a higher chance of having an autoimmune disease, not necessarily the same as your family member, but it does increase your risk. And that's something that's telling us that there is an inherited risk from this, it's not entirely genetic, because environmental factors play a role as well.

Steven Bruce
Okay. And somebody unknown has asked whether gold is still prescribed for RA.

Robert Moots
It always makes me think of gold finger, Steven, I mean, how, how cool would it be to be given intramuscular gold, you kind of end up thinking about that poor girl that was painted over in gold in the James Bond film. So it's an interesting question, actually, because gold is one of the best drugs to treat rheumatoid arthritis for effectiveness. But it's one of the worst drugs for risk of side effects. So we could really work out what the good effect of gold is and bottle that, put away the problems that gold can cause, it will be a real winner. So it's very, very rarely prescribed now. When I was a medical student, many patients were on gold. And doctors tended to give it until the patient got a side effect, which could include death. These days, I can't think of a single patient who's on gold, because we have lots of good alternatives now, that are also safe.

Steven Bruce
What were the other side effects other than death?

Robert Moots
It can cause bone marrow impairment. So it can cause problems with red cells, white cells, platelets can go too low, it can cause renal impairment. So whenever people came in for a gold injection, which would be initially once a week, and then the gap increased to once every month or two, always urine will be checked to make sure there's no blood in the water, and a full blood count will be checked to make sure there's no cytopenias or low blood counts.

Steven Bruce
Thank you, Claire's asked whether we still think HLA-B27 is implicated in inflammatory problems.

Robert Moots
For sure, Claire, it really is. We don't quite understand why. There's a lot of theories, but HLA-B27 is a tissue type molecule. So that's one of the things we measure when we're looking at transplantation. And looking at people's tissue type is a class one MHC molecule that's responsible for presenting foreign proteins who are not necessarily foreign, but proteins to immune cells to lymphocytes. And it's clear that HLA-B27 is a normal tissue type molecule that many of us will have. But if you do have it, you've got a higher risk of having conditions such as spondylitis. Or if you want to be more accurate, seronegative axial spondyloarthritis, which is a huge mouthful.

Steven Bruce
Oh, well, I interviewed somebody on that term several months, if not a year or more ago, and they insisted at the time that it was spondyloarthropathy, not spondyloarthritis. And that was even more of a mouthful. Especially for simple people like me. Sarah asked about the current thinking on exercise and autoimmune pathologies, and she says that one of her patients recently told her that he'd been advised not to overdo it because he'd further damage the joints. Is that true? The patient hasn't done the exercise since he was about seven. Not that we know how old he is at the moment.

Robert Moots
I'm a big believer in exercise, Sarah, and I think the key thing is not whether you do it or not, but how you do it, and how you pace yourself. If you think about it, Sarah, muscles are made to work, and joints are made to move. If you're not working muscles or moving joints, you run into problems. I think one of the key things is if people have an inflammatory arthritis, it can be sore to do that. And I think it's important to be able to teach people about joint protection. And about the best time to exercise. It's not the sort of thing that one would do during an active flare of inflammatory arthritis. But when that flare's being controlled, it's very important to be exercising, so you can build up muscles, protect the joint and maximise function for the future.

Steven Bruce
So what would your advice be then, to this patient of Sarah's, who's not done any exercise since he was seven, I mean, presumably, you don't want him out, sort of exercising to excess, there has to be a point where you say, you know, enough is sufficient.

Robert Moots
Well it depends how old he is now, he could be 17, 27, or 97. I don't know many people who don't actually feel improved, better, and more healthy, if they're able to exercise. The problem is, Claire's patient, if you've never done it, it's quite hard to motivate people to do it, it's quite hard to actually get things going so that they can get out, be in fresh air or in a gym, and actually enjoy the benefits of that. And I think that's really an issue perhaps of us as parents, and the parents of this patient who, maybe for the best will in the world, have tried to protect them if they've had sore joints, maybe had a juvenile idiopathic arthritis, and really, perhaps urge on the really exaggerated side of just protect yourself, don't do anything. So managing that I think is a really big challenge. And there's a whole range of ways that one can try and

overcome that. And in a young person, it can be having video games that are actually linked into movement. And certainly, there's a professor in Liverpool that's developed a video game called, I think the Goblin Post Office for children in the Children's Hospital at Alder Hey, where they'd be playing a computer game with the whole body. And in order to play the computer game, they've got to move around, and that's exercising, but they probably wouldn't realise it. And it seems to have really good outcomes.

Steven Bruce
Okay, so we'll recommend the Goblin Post Office for Sarah's patient and see what happens. Pierre has asked about hereditary traits and whether anyone can develop rheumatoid arthritis or rheumatological conditions? Or do you have to have some sort of hereditary trait? And also, could you also expand when you've done that on the medication you mentioned for osteoarthritis earlier on?

Robert Moots
So Pierre, it's clear that there isn't a genetic inheritance risk for rheumatoid arthritis. And we can do these things called GIWA studies or genome wide association studies where we look at a huge population of people with a particular disease like rheumatoid arthritis and see how the genetics differs. So we can see a few hotspots of genes that seem to be linked with rheumatoid arthritis. On the other hand, we look at identical twins. And if we have two identical twins, the risk of one of them having rheumatoid arthritis means the risk in the other one is about a third. So in other words, if you've got the same DNA as your identical twin, you only have a third chance of having the disease, but a two thirds chance of not having it. So that's really telling us that the genes can be important, but we also need environmental triggers. And for a long time, people have wondered what the trigger would be. There's a thought that smoking, cigarette smoking, could do that. And there are lots of links between pack ears. That's a cumulative exposure to cigarette smoke, and the development of rheumatoid arthritis. So there's some kind of smoking gun, pardon the pun there. The other thing would be infections. And since we know, rheumatoid arthritis and other autoimmune diseases are caused by the immune system going a little bit haywire. It stands to reason that things that might stimulate the immune system might trigger that off. But the problem is, nobody's ever found the infection that causes that. So with regards to inheritance, it's a multifactorial thing. With regards to environmental triggers, we really don't know.

Steven Bruce
That's interesting because Helen asked which environmental factors were most likely to be a problem and what advice you'd give but are there any that you can identify other than smoking?

Robert Moots
I think a good thing, Helen, would be to not smoke or to advise your patients to not smoke. I think that's a no brainer for all sorts of things. We can't advise people to be away from any micro organism or infection, otherwise, we'd be just locked up in a kind of a sterile bubble. So really, we can't answer that. One tantalising thing, though, is that, if people have a Mediterranean diet, which I don't think just means plenty of red wine with your meals, although that could be a very nice thing, but actually olive oil, fish, the type of things that people eat more on the Mediterranean than perhaps here in Liverpool, that's associated with a lower risk of rheumatoid and also less severe disease. So perhaps one thing that we can advise people is to have a healthy diet. But exactly what type of a healthy diet, we're not entirely sure about.

Steven Bruce
Rob, we're going to ignore your racial slur on the Liverpudlians around you. I'm curious, though, because whenever this sort of thing comes up, are we talking about an association between Mediterranean diet and good health or a causal relationship? Because most people who use a Mediterranean diet are probably very interested in their own health, aren't they?

Robert Moots
Yes, I think there is some scientific evidence that if people change the diet to a Mediterranean diet, their rheumatoid can statistically improve. It's not a cure, but it does seem to be a measurable difference. And that's a kind of a important thing. On the other side of that there are a lot of people that make a lot of money, sadly, from advocating very dangerous diets, where there is no scientific evidence whatsoever, either theoretically, or practically, that excluding certain foods can help, but again, a lot of people talk about, for example, excluding inverted commas, acids, or tomatoes, or onions, or perish the thought curries, which is perhaps my favourite food, I think life would be too short not to be able to eat any of that. And there's no evidence that those sorts of things do any harm, with the exception of curries, which is the opposite. There are various components of the herbs in curries and the spices that may well benefit people. So that's another good reason to eat curries.

Steven Bruce
Well, that will be music to Victoria's ears, because she's asked what your view is on natural approaches for inflammatory pain, such as curcumin, if I pronounced that correctly.

Robert Moots
So by natural products, it's a difficult one to answer, Steven, in some ways, because I think we have to be looking at things that can be helpful and complementing treatment, because I don't think there's really any way around a good medical treatment. Although there are various diets, we should claim to do that. I think looking after yourself being healthy, being careful to eat well, is helpful. But it's an incremental help, rather than a kind of a quantum help, as far as the evidence seems to go. So being healthy, eating well, looking after yourself. Again, it's a no brainer, you'd expect people to feel better. And indeed, studies show that they can do.

Steven Bruce
Well, on the subject of nutrition, I noticed one of your areas of expertise is vitamin D deficiency, which is interesting for Joffrey he says he can't go out in the sun because it gets prickly heat. And Jason has asked about vitamin D, he wants to know your opinion on the effects of vitamin D on inflammatory levels in the body and the link to inflammatory conditions.

Robert Moots
Well, there's a clear correlation between vitamin D deficiency and immune system function, so vitamin D has a whole range of things. And in recent years, we've found how important it is in the immune system. It's also important to remember that once you get north of Watford, in the UK, there's probably not that great sunlight to be able to have good vitamin D levels throughout the year. So the vast majority of the UK population will probably be seasonally vitamin D deficient. So I'm a big advocate for taking supplements of vitamin D. Interestingly, I was getting some lectures and Kuwait, which is the hottest

country on the planet. A vitamin D deficiency is absolutely rampant there for the simple reason it's so hot, and so much sun that people cover up all the time, so that they don't get, despite all the great sunshine, enough vitamin D on the skin. In the UK, we kind of expose ourselves within kind of sensible limits all the time when a little bit of sun comes out. But in the latitude North where we are, that quality of sunlight, apart from a month or two in the summer probably isn't enough. So I would certainly advocate to everybody, be careful about having vitamin D supplements. As long as you don't take a bucket full, it's not going to do you any harm, and it's only likely to do you good.

Steven Bruce
We actually had a chap called Simon Billings on the show some time ago, he's one of several who've talked about vitamin D. And he was saying that half an hour in the summer sun with a reasonable amount of skin exposure gets you 10,000 international units equivalent of vitamin D in the body. So it's actually very hard to overdose on it, as you say, unless you're going to take bucket loads of the stuff. But I mean, but all the people who've spoken about it have said that the NHS recommended, or the national recommended daily intake is very low, and in fact, probably should be exceeded.

Robert Moots
Indeed, and the jury is still out as to exactly what the threshold should be. With regards to supplementation. Given as you're quite rightly saying, Steven, it's hard to overdose on it. I mean, obviously, within limits, I think it's good to be taking it, and my wife certainly made sure that I have plenty of vitamin D each day, which is very thoughtful and nice. And also, I think, extremely sensible.

Steven Bruce
Now, I've had a couple of questions in about psychological components in autoimmune diseases, one from David, one from Pip. Pip asking whether stress is a big potential trigger, and David saying that psychological trauma he's heard can be a factor. Any evidence for that that you know?

Robert Moots
Absolutely, David and Pip, you're both entirely correct, both from a stress angle, and a psychological angle. And many years ago, people and patients would always say that some diseases they felt were triggered or caused by stress. And I think many doctors sort of poo-pooed that, and I think you've got to be an arrogant doctor, or rather a very blinkered doctor not to be listening to your patients. And since patients are consistently saying these things, I think there's going to be something in it. And what we found as the time goes by, there's a very close link between the brain, between the endocrine system, for example, the adrenal glands that will make natural cortisone and steroids, the pituitary gland, and also the immune system. So alterations in the stress in the body are likely to impact on the immune system. So there's actually a scientific rationale for that. And certainly, many years ago, we published on a drug that was used as a major tranquilliser for people that are psychotic. And we actually found that that actually had an impact on the immune system itself, in a bad way. So certainly, we have learned that in many things, not just natural stress, but pathological brain problems or psychiatry problems, that there is an interrelationship of what's going on in the body. And that kind of makes sense, doesn't it? Because being healthy, you have some people who have such a positive attitude for life that they seem to just sail through without any problems at all. Maybe part of that is that by being stress free, by being positive, by

having such a good outlook, they perhaps minimise some of the immunological problems that can otherwise cause disease, who knows.

Steven Bruce
I'd say, there's a certain amount of stress in my chair at the moment. So a quick note for my team, could you please cut down the number of questions in my active questions column, because I can't keep track of them. But a number of them have come in with green flags on, which means I've got to ask them straight away, and they're all about diet. Simon wants to know what happens if you can't eat well, if you're allergic, for example, to cruciform vegetables. Am I getting outside your area of expertise in nutrition here?

Robert Moots
That's really tough, and you would have my great sympathies with that. However, it's interesting that allergies to foodstuffs and in the GI tract is also telling us something immunologically about what's going on. So again, there is actually a close interaction between the bowel, the immune system, and not least, the joints. And you probably will be familiar with the concept of the microbiome. So when we look at, if we were to chop me up into little pieces, and extract all of the DNA in my body, probably a minority of the DNA would be from me, and the majority of the diverse types of DNA will come from different species, particularly bacteria. What we're learning in the last recent years, is that the actual bowel has got its own bacterial coating. And that can impact a lot on our health, or on disease. Also, in our mouth, in all sorts of other places. The actual normal bacteria, we call it the normal flora, are actually really important for health. That's one of the reasons that we find that in more recent years where children don't tend to play outside so much, where everything's very sterile, people don't get exposed to a whole variety of microorganisms. The rate of some autoimmune diseases has actually gone up. So I think it's very important to have a concept of good bacteria, as opposed to bad bacteria. And when people have got a food allergy, and that's going to do a number of things, not least alter the bacteria in the bowel. So one of the tricks I think, will be to try and find alternative foods that are tolerated, that are still very nutritious, but don't actually cause that and can be beneficial. So you've got my sympathy, if you have a food allergy, and it's making your life a little bit miserable.

Steven Bruce
What about B12? What's the role of B12 in autoimmune problems?

Robert Moots
I tend not to think much about B12 in autoimmune problems, I can see it as a component of an autoimmune response that actually prevents absorption of vitamin B12. But to me, B12, is much more relevant with regards to synthesis of blood. So autoimmune problems can minimise the absorption of B12. And therefore, people may need to have a vitamin B12 injection every few months. But I don't see that there's quite the same link of vitamin B12 in the immune system in the opposite direction, as for example, vitamin D in the immune system.

Steven Bruce
We're back on vitamin D and I have been asked if you've got recommendations for a daily dose of vitamin D, but more specifically than mine, don't eat too much and yours don't eat bucketloads.

Robert Moots
I wouldn't like to sort of comment directly on that, as I wouldn't like to give you kind of a top of my head recommendations. I forget whether there are units or micrograms or milligrammes. I think my wife gives me about 1000 of something. But exactly what the units are very important. So you can go into your local chemist, and just buy a box of vitamin D supplements, it will come in two or three different strengths. I think all of those will be pretty safe to take. But I would recommend that you check upon that and don't totally overdose yourself. And I would feel really guilty if I caused you problems.

Steven Bruce
Yeah, well, I would say if you really want to know something about safe levels of dosing for vitamin D, then look at the broadcast we did with Simon Billings. I think it's about vitamin D deficiency, I can't remember the title now, but there's a lot of detailed information in that one. Lisa says that she has a patient who has ankylosing spondylitis, rheumatoid arthritis and ulcerative colitis. And she wondered how rare or not this was in light of you saying that one can lead to another.

Robert Moots
The combination of those three problems would be excessively rare. I would even contend that perhaps at least one of those diagnoses possibly may not be correct. Certainly, ulcerative colitis, inflammatory bowel disease is highly correlated with conditions such as ankylosing spondylitis. So that is no surprise whatsoever. But immunologically, those diseases are very different to rheumatoid arthritis. So what may be the case is that somebody has what we call seronegative inflammatory arthritis. Because there are forms of, for example, psoriatic arthritis, B27 related arthritis, but clinically looks like rheumatoid arthritis. So you know, you wouldn't necessarily tell, because it looks the same, but it would be a different disease. So if you do have all of those three diseases, then you'd be extremely unlucky, but if the diagnoses were challenged a little bit, it may be that there's only two of them but not the three.

Steven Bruce
Okay, so encouraging then for that particular patient. We're going to come on to ankylosing spondylitis in a minute, or ankylosing spondyloarthropathy, or whatever we're going to call it. But just before we do that, I'm dragging you back again to neutrophils. Matthew's asked whether they're involved in inflammatory bowel disease and hence is there a link between inflammatory gut diseases and rheumatoid arthritides? In other words, is there a strong link between angry guts and angry backs etc. I liked the way you put that, Matthew.

Robert Moots
Yes, I like that too. And the short answer is yes, we do know that in some forms of inflammatory arthritis, it's much more prevalent in people with inflammatory bowel disease. And we don't know whether that's caused by neutrophils themselves, or whether the fact that inflammation in the bowel allows various bacteria to get inside the body in an abnormal way and actually stimulate an abnormal immune response. It tends not to be the case for rheumatoid arthritis being related to that. But for a seronegative that means rheumatoid factor negative arthritis. For example, ankylosing spondylitis, psoriatic arthritis, all of those things that tend to fit with HLA-B27.

Steven Bruce
Okay, and then hopefully for a little while anyway, the final question on RA, and you might actually have answered this one earlier. I'm sorry, if I'm asking you to repeat. Dawn's asked whether we understand why one person might develop auto antibodies against their own cartilage cells, while another person might develop antibodies against the thyroid and get Hashimoto's for example. Is it a mix of environment and genetics, and so difficult to predict?

Robert Moots
Well, I think Dawn, the person that could answer that will get a Nobel Prize, because that's one of the key unanswered questions that we have at the moment. It's very exciting that we've made big advances. But once you make a big advance in one way, it actually uncovers another question in another way. And lots of these questions are very tantalising, because it's clearly going to be telling us something if we can answer it. But many of those we haven't actually answered yet. So that's a good example, Dawn, of why we actually see these kinds of things. But we can't honestly explain, we can concoct potential hypotheses. But the truth is that we don't know.

Steven Bruce
You won a lot of prizes and awards, is the Nobel on your target list?

Robert Moots
Not even in my dreams, I'm afraid, Steven.

Steven Bruce
Okay, so ankylosing spondylitis. Pip says, Is there any particular statistic for how many people with AS are HLA-B27 positive? She has three direct family members who all have AS, and they are negative. And she has been referred to rheumatology for possible AS as well. And she's also B27 negative?

Robert Moots
Well, I think, Pip, that's a very interesting family. Because there are HLA-B27, I can't quote the precise figures, I would just be guessing at it, but you're looking at maybe about 15% of the UK population would have HLA-B27. But the actual incidence and prevalence of ankylosing spondylitis is far lower than that. So just having the gene doesn't actually mean you're going to get the disease. And conversely, if you don't have the gene, it's actually very unusual, rare to actually have ankylosing spondylitis. So that's a little bit of a paradox. What that's suggesting your family where there are three family members, if they've got definite clear disease, with either MRI, or radiological evidence of say, sacroiliac joint involvement, that would be telling us that there's a different gene that's involved in that particular family. And certainly, people used to think that in Africa, various parts and Sub-Saharan Africa where HLA-B27 was pretty well unheard of, they would never get ankylosing spondylitis. But the truth is, you can do, maybe not quite as prevalent. So there is the possibility, rarely, but definitely as you found Pip, of having HLA-B27, if you're having AS if you're HLA-B27 negative. And again, just like AS when B27 positive, that tends to run in families. And what I always like to do is to advise if somebody has what could be inflammatory back pain, so that would be lower back early morning stiffness, ask about other members of the family with back problems that I'm sure would be a knee jerk response for you. But it can be very illuminating. Because you often find whole members of the family, more likely men than women, but these days we're finding

AS is far more prevalent in women than we previously thought. It just manifests slightly differently with slightly different pain and stiffness, it's not as common as in men, but it's more common than initially thought.

Steven Bruce
Is there any relationship between positive or negative HLA-B27, then the severity of the disease?

Robert Moots
No, it's not in the same way as rheumatoid factor, the antibody in rheumatoid arthritis, that does correlate with severity of disease. B27 positivity or negativity doesn't tend to correlate so much with regards to severity of AS.

Steven Bruce
Okay. Lucy's asked about whether there are any new approaches to diagnose or treat ankylosing spondylitis?

Robert Moots
Well, Lucy, there have been lots of revolutions in treatment over the years. Funnily enough, many years ago, one of the big revolutions was understanding about the role of physical therapy, exercise, and moving joints and backs around because once we realise that if you don't move the back, it gets stiff and then doesn't move at all. Whereas if people have regular exercise, puts the back through a whole range of different movements, that minimises the actual impact of progression of the disease. So the first revolution was just understanding, keep people moving, keep them exercising, and bully them in a nice way to keep those backs moving. I think the second revolution was understanding more about non-steroidal anti-inflammatory drugs. Because these can be very good painkillers. They're not really anti-inflammatory drugs, they're more kind of painkillers that are useful for musculoskeletal pain. But these can actually revolutionise the management of AS, and particularly the coxibs. And one of the drugs that I find the most useful is Etoricoxib or Arcoxia. Many patients find that that can work when other NSAIDs don't. And funnily enough, when we look at the other coxibs, Celecoxib, there are actually some studies to show that good doses long term of Celecoxib can minimise progression of disease. And that's again, very tantalising because other drugs tend not to do that. And then, finally, Steven, the new generation of biologic drugs, these are the targeted drugs. In rheumatology, we've stolen drugs invented to treat one disease, and we've used them to treat a totally different disease, we've not really know why we're doing it, just it seemed to work. We're cheap and cheerful. We're always cheerful, because we have chronic diseases, but we used to be always cheap. But then the final revolution, as I said, was the development of very expensive targeted drugs. And those have come about because we've understood the science underlying the disease, we've understood about the inflammation pathways, and that's led to the development of drugs that will target the inflammation in very specific ways. And we now have a variety of different targeted therapies, we have the TNF alpha inhibitors like Humira, Ambril, all those sorts of things. We have other drugs that target a different cytokine, or inflammation chemical, the IL 17 inhibitors, and these are things like secukinamab, which are very, very effective in many people. And then whilst those two types of drugs are proteins, they tend to be antibodies, so we can't eat them, we have to inject them. The third type of drug, or what we call the JAK inhibitors, or janus kinase inhibitors, and these are things like tofacitinib, baricitinib, and all those things, which are small molecules, therefore, you can take

them as tablets, rather than injecting them. So over the years, each one of those three broad changes have really made a big impact on patients. Because at the end of the day, with AS, it's typically 12 years before patients get a diagnosis for the onset of symptoms, it's a long time.

Steven Bruce
And so what then in terms of overall prognosis has changed, they get diagnosed earlier, they're getting new biogenetic drugs and so on, what's changing for their quality of life?

Robert Moots
Quality of life has transformed. And that's for a whole variety of ways. It's increased function, it's reduced pain, and it's improved kind of feeling of pep, and activity, and awareness. And it's not just those kind of patient reported outcome measures that we see change. We even see people, typically an older man with ankylosing spondylitis would have a very hunched spine that was kind of fixed like that, you would expect there to be no chance of any improvement. But a small number of those people on a targeted therapy with a TNF blocker, can actually straighten up. And it's really marvellous to be able to see the impact that those have on people's ability just to lead more normal lives.

Steven Bruce
And do those drugs carry with them any or many adverse effects?

Robert Moots
Well, we used to be very scared. I've been using TNF blockers in my patients for the last 25 years or so, since I was at primary school. And one of the big things about these drugs, they're called tumour necrosis factor inhibitors for a good reason. And that, the chemical, TNF, will actually spontaneously kill cancer cells in a test tube. So therefore, if you're going to chronically inhibit this chemical, which we know in the test, you can kill cancer cells, we've worried that it's going to make people more susceptible to developing cancers. And also because that chemical's important in defense against infection, we've worried that they're actually going to just cause loads of infections. So when these drugs first came out, I thought they were just going to be too toxic. I couldn't have been more wrong. Because over the last 25 years, we've shown very clearly, both in clinical trials and also real-life registries that although the TNF blockers increase risk of infection, it's easy to detect, easy to treat. And it's not the worry that we thought. And there's absolutely no risk that we can see of actually increasing risk of cancers. So strangely enough, these drugs where we're inhibiting important chemicals through inflammation, the long-term outlook, the long term impact with regards to side effects is far, far better than we ever actually predicted. So don't take any tips from me for the future because I would have got it totally wrong for the TNF blockers.

Steven Bruce
In terms of diagnosis, Rob, the NHS changed its guidelines some time ago, didn't it? And it now has the NICE guidelines, but if you had back pain, since you're under 45, and it's gone on for longer than three months, then if you've got three or more of the symptoms on the list, or signs on the list, then you should be referred to a rheumatologist for assessment for ankylosing spondylitis. Now, and I'm not going to read out the the list of symptoms, but you can find them and it's interesting because there's a letter which has been produced by the National Association for Ankylosing Spondyloarthropathy, I think is the full name, the NAAS, there's been a letter produced by them, which is signed off by the RCGP, the Chartered

Society of Physiotherapists, the Royal College of Chiropractors and the Institute of Osteopathy. But it caused me a little bit of concern when we interviewed somebody about this because they give a template letter which we could send to our GPs, if we have somebody we think might have AS. And they say that the NICE guidelines say that because we've ticked all these boxes, we should refer to rheumatology. But when I went through the list on the template letter, it differs from the NICE guidelines. Now, perhaps I'm just being pedantic and picky, why would I ever, but I'm just thinking, if a GP spotted this and thought we were trying to farm somebody through for expensive tests, on the basis of evidence, which wasn't made available to NICE, would we be in trouble for that? Or is it just, the best thing is just get as many people through for assessment as possible.

Robert Moots
I think the key thing here, Steven, is to use a bit of clinical acumen. And I think that's where, if you're trained appropriately, if you've got the right level of experience, if you talk to and listen to your patients, as I'm sure you do, not just going to be ticking things off, but have a little bit of clinical acumen with regards to how you'd interpret that. And it's always a difficult thing with these algorithms for referral. Because usually algorithms, I think, to work best require a little bit of clinical knowledge. And critical thought. So if you use that, then you won't be sending so many people unnecessarily, I think we have to accept that sometimes you have to kiss a few frogs before you find a princess. And that's not necessarily a bad thing. Because I would rather see somebody and rule out the diagnosis, rather than have somebody walking around and never get diagnosed, because people don't think about it. So you guys are in a great position to be seeing people, thinking critically, and actually filtering them through. So that's a really crucial role, I think.

Steven Bruce
Well, I suppose actually that was probably the main point of my very long winded question there. It was just, I don't want my profession, and I'm sure that the same goes for chiropractors and physios, we don't want anyone to hold our professionals to account because we've misquoted the NICE guidelines or something like that. But if you are interested, if you go to the National Association for Ankylosing Spondyloarthropathy's website, NAAS and you go to the professional tab on their menu, you can find the template letter which you can download and it comes with all these badges at the bottom to impress your GP and you can tick the boxes to say this is why I'm referring the patient, which means I have a much better chance of reaching someone like you, Rob. Good. I'm glad we cleared that one up. Pierre has asked another question, a very broad one he tells me and maybe opening Pandora's Box, Pierre, I know you well, not you, surely. He says, Pierre is actually a physiotherapist, and he says that as non-rheumatoid disease experts, have you any advice for us to identify and therefore orientate patients to the right service. He is particularly aware of conditions like scleroderma, vasculitis and juvenile conditions.

Robert Moots
Absolutely, Pierre, I think you can play a huge role in this because you will not just be focused exclusively on the musculoskeletal system, but you can pick up other signals, other symptoms and try and look at the whole person, rather than just focusing on a gammy knee or a gammy shoulder or whatever. Certainly, there are some signs, we talked earlier about the photo sensitive skin rash in lupus, that can be easily detectable, particularly if you're seeing a patient on a sunny day. I think there are also things, such as the very tight hard skin that people with systemic sclerosis scleroderma get. So again, when

you're examining patients, you'll be looking not only at the point or joint that's playing up, but have a wide angle lens and just look at the whole patient, maybe not so much in huge great detail. But if you can pick up these little teasers, these little physical signs, then I find that physiotherapists have extremely good at thinking about all of these things. And of course, within the context of our service, we have extended scope physiotherapists, who are effectively replacing primary care doctors in many ways with regards to musculoskeletal problems. They spend time in our department, seeing other types of rheumatology problems, and we will get referrals from them for a whole range of diseases. And that's something that I think we should really welcome.

Steven Bruce
I'm going to be very rude, Rob, could you possibly run through that again? Because the stream I'm told froze at that point. Back to Pierre's question, which is about advice for us and identifying and orientating patients. If we just hang on for a second, the stream I'm told is still frozen. I don't know why. Justin, can you tell me anything? Okay, well, I mean, if the stream has frozen, then people will be able to pick it up on either the transcript or the recording. So let's leave that for the moment, I think. I'm still being told that the stream is frozen, so I'm going to shut up just for a second.

Robert Moots
It's usually the lens of the camera that breaks when I'm in the frame. But I'm not actually knowingly caused a frozen stream before.

Steven Bruce
I'm not actually sure who is telling me the stream is frozen, so it may just be for them. So Justin says that we're still streaming.

Robert Moots
Well, I think either way, Pierre, have a wide-angle lens, look at the whole person, think about all the other things that might be going on. And please be very forward in suggesting things that might be going on, alerting the relevant medical staff. And early diagnosis can be a very important benefit to the patients that you've seen.

Steven Bruce
I just realised there's another one here from Pierre as well, but it's connected to a further question. Nicholas has asked whether you are based up there in Liverpool, because there is statistically, the area has more patients for you to study for your team. A greater than average percentage as in the rest of the country, maybe even Western Europe. Are autoimmune conditions affected by atmospheric changes? Sorry, I was trying to make sense of the question which is...

Robert Moots
So, it's interesting. I don't know if you've heard, Steven from your patients. But all patients seem to actually report that their arthritis is worse when it's cold, or when it's raining. And you can almost imagine human barometers that by how the joints feel, you can tell what the weather is going to be like. And so many patients say that. Funnily enough, studies have been done, correlating patient's symptoms with barometric pressure, and with rainfall. And crazily, there's no correlation whatsoever. So, something

perhaps we're asking the wrong question scientifically. Because so many people will report things are worse in the bad weather. On the other hand, everything's worse when it's raining, isn't it? I mean, certainly in the northwest, we have, you know, a fair share of rain. Although strangely enough, the prevalence of rheumatoid arthritis is not particularly higher than in other places. People do say that some autoimmune diseases are a disease of relative poverty. And certainly, funnily enough, in the northwest, you get some of the richest postcodes in the country, but many more of the most kind of humble or less well funded postcodes in the country. And certainly, disease is far more worse there. And it's very interesting, the concept of health and inequality. That's something that's on the research agenda in many places with that. But I don't know I ended up in the northwest to be honest. I'm happy to be here. It's good to be in the Northwest. Patients certainly need me, so at least I feel useful. But whether or not it's because there's an excess of the patients that I particularly have an interest in diseases. I can't really pretend that.

Steven Bruce
Well, that other question I mentioned was actually about EULAR, which I forgot to mention in the introduction that the centre you've set up in Liverpool is a EULAR Centre of Excellence for rheumatology, isn't it? I'm going to have a stab at this, European Lead Agency For Rheumatology, is that the acronym?

Robert Moots
It's recently changed its name, it used to be called the European League Against Rheumatism. And now it's changed to European Rheumatology Associations or something, the bottom line is, it's to do with rheumatology joint problems, and is a European body. And every now and then they badge various centres to be so called centres of excellence. And it just shows you can fool some of the people some of the time.

Steven Bruce
Well, PSSC has been looking at EULAR courses on rheumatic diseases to develop his own knowledge. And do you have any views on the courses and what might be useful?

Robert Moots
So I'm not sure where you're based, Pierre,

Steven Bruce
He's based in the Midlands.

Robert Moots
So Pierre, there are two things. EULAR set up, a few years ago, some very good educational, and endeavors and things. And they do a variety of courses, a variety of training things. However, also, I would very strongly recommend the British Society of Rheumatology courses, the BSR runs a hell of variety of courses, they're highly rated, extremely relevant, practical and accessible, and I would see the quality of the BSR courses, at least as good as the EULAR courses, in some cases better. So you've got a nice broad choice really, a British led course, a European led course. Either way, these are all things which are great because they should be run in an accessible way, an interesting way. And we can all learn a lot from all of that.

Steven Bruce
I love this. We're asking a Frenchman to choose between a European course and a British course. Fantastic. Pierre, I look forward to hearing which channel you went down. Emma's got a problem with a patient. Emma says that she has a patient who she thinks possibly has AS, ankylosing spondylitis, but she can't get a rheumatologist referral. The patient's been diagnosed with fibromyalgia, which is managed by GPs in the area, any hints as to how to get a referral, she's on several major painkillers, but still in pain.

Robert Moots
I'm very disappointed to hear that you've got this situation with your patient, because patients have a right to be seen by an appropriate health care professional. So if they're not being seen by a rheumatologist, then the number of possible underlying reasons clearly, I don't have a situation so I couldn't comment. And I would hope it's not that the GP feels that they know best and wouldn't want to get her any help. I would also hope that it's not the patient that's perhaps misunderstood the explanation from the GP about what is wrong with them. I mean, fibromyalgia syndrome is a very challenging disease to manage. That doesn't involve inflammation. So as you can imagine I'm not perhaps one of the best people at managing that, although I have to say I find myself on a Royal College of Physicians Working Party on FMS, so I seem to get everywhere really. I just need to learn how to say no, Steven. But the difficulty is that fibromyalgia syndrome is very, very different. As you know, from ankylosing spondylitis, it doesn't cost much to do a simple Xray of the pelvis or sacroiliac joints. And in most patients that would show up something. The GP could do that, they don't necessarily need to see a rheumatologist. But as you probably know, that there's a concept now of non-radiographic AS. So in other words, it's active inflammatory disease. But because the Xray changes happen late, it's now diagnosed on MRI scans. And in some situations, MRI scans of sacroiliac joints in the spine could only be done within the context of secondary care, not primary care. So the first thing would be to try and persuade the GP to do a couple of simple little tests. If they're positive, the GP will be a little sheepish, because clearly there's something going on. If they're negative then that shows it's less likely that there is a problem. Not impossible. Again, it could be that the patient may want to change GPs, because again, either they're not being referred appropriately or the GP is not able to explain clearly in an accessible way, what's going on, and why it maybe it isn't ankylosing spondylitis.

Steven Bruce
Right. Thank you. Just on that subject, I might have actually covered this enough in a previous section. But I'd recommend looking at that NAS website for the format letter, which gives what it says of the NICE guidelines. I mean, if you sent a letter to the GP which said, these are the NICE guidelines, I've ticked them off. And it also refers to the spade tool. And Matthew, I know you said that I was talking about the spade tool I wasn't, that was separate. But there's a reference to it on that letter, you can tick the boxes on the spade tool, which is all giving evidence and applying a little bit of pressure to the GP to get that evaluation done. Can you tell us a bit more about the spade tool?

Robert Moots
I'm not terribly familiar with that, actually, that's not the sort of thing that we tend to be using on a day-to-day basis. So I'd be keen to hear from you, Steven, about that, you can educate me.

Steven Bruce
Well, I haven't used it. But when I looked at it on the NAS website, it seemed to be a number of checkboxes, and if you ticked enough of them, it would give you a score and tell you whether you were likely to be suffering from an arthritic disease. So yeah, I will send out a copy of that letter or a link to the copy of that letter after the broadcast. Well, we kept off rheumatoid factor for a little while and RA, but Amelia says, what's classed as high rheumatoid factor?

Robert Moots
Amelia, how long is the ball of string? It's, to me, it's something that would either be positive or negative. There are different units, in different labs. So different labs around the country would report that in a different way. Certainly, whatever the reference ranges of your lab, the higher it is, the more likely, but not inevitable that it will be significant. But in some ways, if that doesn't really fit with the patient's symptoms, and also with other blood tests, which I find more useful, such as the CRP and ESR that are measuring inflammation. If the CRP and ESR are normal, and if a patient's not got inflammatory type symptoms, then I wouldn't be worried about it. Similarly, if somebody's negative rheumatoid factor, but they've got inflammation in the blood, they've got sign of itis, early morning joint stiffness, then, irrespective of the rheumatoid factor, it's going to be important to get those people assessed. So don't worry too much about the absolute level. Although the higher the level it's slightly more likely that there's something that's going on, but not necessarily inevitable.

Steven Bruce
Thank you. Gaminda has asked again about RA, is he right in saying that RA afflictions are affecting the Asian population far more now than 20 years ago. You hardly heard of it in Asians, but now it seems far more prevalent, even in young Asians. Why is it becoming more prevalent, if that's the case? Could it be low vitamin D, or inflammatory triggers or other factors?

Robert Moots
That's a good question, Gaminda, not only in South Asian people, but in people from other countries that are kind of developing. I go across to East Africa a lot, for a variety of reasons. But it used to be that rheumatoid arthritis was so rare in East Africa, that if you saw anybody with it, it would be a case report. But now, there are rheumatologists around that region, we find the prevalence of rheumatoid arthritis is a little bit lower, but not far off what it is in the UK. And certainly some of it may be just a lack of visibility of this in healthcare facilities able to diagnose it. I've been going to India also for many years and helping out with rheumatology and other things over there. And there's clearly, to me, a lot of rheumatoid arthritis there. So, whether or not it was not really quite as visible because other diseases had all of the attention, I think certainly could be the case, but also we tend to find that rheumatoid arthritis is a disease of industrialised countries. So for example, in rural Kenya, there was not much rheumatoid around until there started to be urbanisation. And then there was more of it. So whether or not that urbanisation tends to, you know, relate to smoking, or there's some other environmental factor there, but I think you've made a good observation that perhaps this wasn't a big issue in the past, but certainly is an issue now. Exactly how, I suggested a couple of things but the truth is, we don't really necessarily know.

Steven Bruce
Some more questions about diet for you. I don't know who's asked this one but they put in some long words for me to tangle with. Have you reviewed research on mycotherapy, adaptogens, such as the answer inflammatory Ganoderma lucidum or Reishi fungus?

Robert Moots
Short answer, no. There's many different types of dietary manipulation, some tend to become very popular at some stage and then fade and wane away. Others tend to become more popular at other times, so I don't keep track of all of the various things. And I'm not aware of that I do apologise, I can't answer that.

Steven Bruce
Any information for Laurece on probiotics?

Robert Moots
Probiotics, I think the things that would relate to what I was saying earlier about the microbiome. So what you're doing is trying to influence the bacterial flora of the bowel in a way that can be beneficial to the immune system, there is no doubt that that can be helpful. The trouble is, we don't really know exactly what the beneficial thing is. And it's really scary, because there's lots of research now, that's going on looking at the concept of faecal transplant, which, after dinner is not maybe something we need to go into any huge, great detail. But it does involve having, thankfully, in a tablet form some of the kind of faecal bacterial material that might actually help grow and develop beneficial bacteria, whatever they may be. I think that this is something that in the future, we'll be hearing more about, and perhaps do it in a little more targeted and perhaps pleasanter way.

Steven Bruce
It's a curious thing, isn't it? I've always wondered why my dogs are prepared to eat other animals poop. And I haven't researched it in any great depth. But I do remember reading something by somebody based on no research whatsoever, which said they were trying to supplement things and I don't know which things, vitamins, minerals, and whatever that their body knew it was deficient in. So maybe they're ahead of the game there.

Robert Moots
Well, I've got two dogs, they're Hungarian vizslas or celcro dogs, as people often call them. And what I can really not understand is how dogs can have such a sophisticated sense of smell, that these days they can smell COVID in an airport waiting queue, but still will eat the most revolting things. It's just, I can't understand that. My daughter's a vet so I should probably be asking her.

Steven Bruce
Well, Pep's just sent in an observation, her husband has apparently been on Humira for his psoriasis. And she says it was amazing. He's been off it for the last four years or so and hasn't really had any major returns to how he was, just small bits here and there. She says it's brilliant.

Robert Moots
Yeah, that's such good news. Because what we really want to do for these autoimmune diseases is to cure them. What we do, normally, is to control them. So a little bit like diabetes, if you have type one diabetes, you take insulin, you live a normal life with the insulin, but stop the insulin, the disease comes back. So similar in autoimmune diseases, when we actually treat with any kind of disease modifying drug, even methotrexate, they can often control the disease. But when you stop, the disease flares up. However, in a small but significant proportion of people, stopping the drug means the disease doesn't come back. And I just wish that happened more often. So I think her husband is in a really nice position that he's had a drug, it's worked well, he's well without the drug. And I guess where it's at other flare up again, he could go back on a drug that he knows has worked, and it should work again.

Steven Bruce
Lawrence obviously has a particular interest in probiotics. He says that the APC department of UCC here in Cork, he says, has developed a probiotic called bifidus infantis 35624, nice name, which trips off the tongue, which is apparently effective in helping IBS conditions.

Robert Moots
That's great. Does he have shares in that?

Steven Bruce
I don't know. I don't know. Tell you what, though. Can I drag you back to vasculitis? While we still got a few minutes left. Because what we haven't talked about is polymyalgia rheumatica. And you probably know a hell of a lot about that. And yet, I know that in many cases, it's quite hard to recognise sufficiently early in patients, what should we be looking for?

Robert Moots
So I'm really glad that you asked that, because that's something where it can present to a whole diverse group of clinicians and people tend to present with what's often mistaken to be joint problems, and issues lingered or problems around the shoulders, around the pelvis. And what I like to ask these patients is three things. Number one, what's it like getting out of the chair or getting out of the car? Number two, what's it like lifting heavy things down from above your head? And then the third thing, which is actually very discriminating I find, can you roll over in bed without having any problems? So obviously, there are many joint problems that would cause some, if not all of those things, but you'll all be able to examine joints, and you'll be able to see whether there's actually a pathological functioning joint, if you examine the joint, and that actually looks okay, but the patients who've got those symptoms, then I really think, as long as the patient's over 55 years old, because we won't diagnose it younger than that, it merits a check with a GP and a blood test for CRP and DSR. If it's polymyalgia, it's curable. It just needs a course of steroids. Six to nine months, patient's cured, stop the drug, and it doesn't come back. Otherwise, it can be months, years of agony.

Steven Bruce
Absolutely. You made a very rigid cutoff point there, 55 years of age, I mean, is there no incidence of it below that age?

Robert Moots
We would tend not to diagnose it. And in fact, the various international guidelines for diagnostic criteria would require the age greater than that. Now, I think for me, one of the key questions is, why? What magically happens, what will happen to me when I ultimately get to the age of 55? If I ever manage to get that way? Why will I get the chance of having polymyalgia? Whereas if I'm younger, I won't? And the answer is, we don't know. However, what we do know is that the immune system changes with age, it doesn't mean to say it's not working. But the way that it works can actually change with age. And that's one of the reasons that we tend to grow out of hay fever in many cases. And that could be one of the things that's telling us why polymyalgia is only diagnosed in people over a certain age.

Steven Bruce
Okay, I've been asked to ask you, obviously, I know the answer to this question. What is DSR?

Robert Moots
DSR, well, I'm really sorry.

Steven Bruce
I thought you said DSR.

Robert Moots
No, ESR.

Steven Bruce
ESR, in which case I think we know, it's erythrocyte sedimentation rate.

Robert Moots
Right? Yes, yes. I'm sorry, I wasn't clear. It's my, my kind of scouse accent, not.

Steven Bruce
There's an interesting question, which is, again, anonymous. Do you ever see things, in referrals from people like us, the physical therapy professionals, where we've got it badly wrong, or not badly wrong, but we get it wrong?

Robert Moots
Absolutely. But then so I do from other consultants, from general practitioners, from anybody. So what I don't find is that referrals that have been triggered by you guys are any worse than referrals that are triggered by other places. In fact, I tend to find that you guys probably are a bit more bothered about trying to get it right. So I find it's actually a higher chance of being right, compared with many general practitioners that, you know, for them, it's no big deal to be referring things on. So I think you can be congratulated as a group that at least in our practice, we tend to see a higher chance of appropriate, good and relevant referrals. But don't let that go to your head.

Steven Bruce
Interestingly, Carrie has come in and said that she's given to understand that it's very hard to get GPs to take the idea of PMR seriously, is that your experience? And if so what's your advice to us?

Robert Moots
If that's the case, that would be quite sad, because it's a fairly prevalent disease. And it's very prevalent in primary care. And it's the sort of thing that we'd like GPs to be trained to diagnose it in the sleep now, hopefully, they'll be awake, but it should be a very straightforward thing. And if, I was having that sort of experience with a GP, then that's sad, really, because it's an easy disease to diagnose. It's just a matter of thinking about it. Because if you think about it, who doesn't get pains in the shoulders when they get beyond a certain age? Mostly, that's going to be due to wear and tear, degenerative problems. But it doesn't take more than a couple of quick questions, to screen out other potential things. And I think it's a shame when people don't think that little bit of a wider context, a little bit of a wider-angle lens. And if the GP's just got about five minutes for a consultation, that's four minutes longer than you need to diagnose polymyalgia, if you think about it.

Steven Bruce
Okay. A couple of questions about drugs have come in, Lucy's asked why her AS patient has been given Gabapentin, and it hasn't helped apparently.

Robert Moots
Well, Lucy, I'd struggle to think of why myself, to be honest, Gabapentin is a very useful drug for pain modification in a variety of conditions. Obviously, it's the kind of drug that we'd use in my practice for things like fibromyalgia syndrome, and other things where there's something abnormal with regards to nerve transmission of pain, where your brain's receiving pain signals when it should really be receiving touch or pressure signals. So, some diseases, this can be great. For ankylosing spondylitis per se, that would not be the type of drug that I would tend to think of as being terribly useful because there are clear mechanical inflammatory problems there. So unless the patient's also got something like fibromyalgia syndrome, or something on top of that, there are other drugs, and NSAIDs, potentially sulfasalazine. If it's peripheral disease, a TNF blocker, or a targeted drug, if it's very severe disease, but Gabapentin would not be at the top of my list for useful drugs, not impossible, but it wouldn't be top of my list.

Steven Bruce
Thank you. And the other one was from Jen who says, she had a patient who was on methotrexate, who stopped after three years, and it never came back. I'm not quite sure what the it was that never came back. But is that common?

Robert Moots
Doesn't matter, but it's good news. And that's one of the things, you can put people on the drug, they can do well, you can monitor them for side effects, and then just forget about them. So what we always should be thinking of doing is, if a patient's well, if they're in remission, if they've been in remission for whatever disease for at least a year or two, can you get away with lowering the dose or stopping it. So that patient of Jen's clearly did. And I think there could be other patients around on drugs that are maybe not doing any harm, or maybe they are a bit, but perhaps they're actually being taken unnecessarily. Most people

flare with inflammatory arthritis, but enough of them won't to make it worthwhile trying. And everybody wants to try and be off drugs if they can be.

Steven Bruce
Well, we got a very few minutes left. And one thing which I know that you also deal with is trigger finger and I thought, well, let's get to the peripheries a little bit and away from all these zero negatives and others. What can you tell us about treating trigger finger?

Robert Moots
Trigger finger I find can be a very challenging problem, strangely enough. The bottom line is, there are a variety of different conditions that can really cause that, but I break them down into effectively two different types. An inflammatory problem, such as rheumatoid arthritis where people get nodules around the flexor tendons that can just get stuck, or degenerative problems, where degenerative tendon sheath can actually cause triggering. Now, strangely enough, I don't see very much of that. Maybe I don't ask about it enough. But in cases of triggering of fingers, then there are a variety of things that can be done theoretically, including getting a physiotherapist to see and assess patients. But the bottom line is that many patients respond to a little injection of some cortisone around the tendon sheath. And that can work wonders for people. It's a very satisfying procedure, quite often. Trouble is, if you get it wrong, and put a steroid in a tendon, you can rupture the tendon, and that doesn't look very good in court.

Steven Bruce
It just occurs to me on the spare of the moment, is there any role for something like shockwave therapy in treating it?

Robert Moots
That's a good question, I don't know. Maybe you should try. Do a little study on it. And that will save people having rotted tendons by people injecting inappropriately steroid around there. I honestly don't know. But it sounds as though it could be worth a try.

Steven Bruce
Interesting. I'll speak to Tim Watson. We're arranging for Tim Watson, who's the ultrasound expert, electrotherapy expert, retired now from Hartford University. But yeah, I'll ask him if he's got any evidence on that. Now, I have throughout my relatively short medical career, I've been calling this Dupuytren's disease or syndrome. And I wonder whether - the rest of the world calls it Dupuytren's as far as I can see. Is there any connection between that and trigger finger?

Robert Moots
Again, that's a tricky one, Steven. Intuitively, it would make sense that you'd see one as the extreme end of the spectrum for another. Funnily enough, I actually hold a grant on examining what the cause of Dupuytren's contracture is, and we're actually looking at the potential to rather than have operations and, I try and keep people away from surgeons, surgeons are good to stay away from if you can do, but we're looking at the potential for injecting things around the Dupuytren's, for example, a TNF blocker like Humira. And that's a little way down the line, but at the moment, certainly surgical treatment, it may be

more medical treatment, and there are things that might make us suggest that it could be part of the same spectrum as trigger finger. So it's an interesting thought.

Steven Bruce
Well, I'm glad I asked that question then. And I chalk another person up who pronounces it the way I don't pronounce it. Pierre, you're French. You should tell me how Dupuytren's should be pronounced, because I'm sure it's a French word originally. Rob, it's been brilliant. And we've had loads and loads of thank yous come in, particularly when the stream froze, and they were just sending in their thank yous for filling the time. We don't have time for an... Oh, do we have time for one more, maybe? Jennifer says, could you explain what a positive HLA-B27 test means? She is currently treating two 25, 26 year olds with AS, one very mobile but positive, one who is very immobile, but negative. I kind of feel that you went through that earlier on, but perhaps you can...

Robert Moots
Yes, I think, Jennifer, the bottom line is that it's not necessarily meaningful at all. If you have the diagnosis, if it is AS, having B27 or not, is not really going to make any big difference. So don't worry about that.

Steven Bruce
Okay, and then Mike has asked about PMR, who decides the level of steroid required, the GP or a rheumatologist?

Robert Moots
Oh, I think it should be a GP, it's very straightforward. If you're not sure, go to the British Society of Rheumatology guidelines for treatment. Effectively, it means you start at 15 milligrams of Prednisolone once a day, and then there's a little protocol to deescalate it and decrease it down to zero over about six to nine months, it's very straightforward. We only see people in secondary care where the diagnosis is a little bit dodgy, or there's something else going on, it really should be treated and managed most effectively in primary care.

Steven Bruce
Brilliant. Rob, that's taken us right up to time, thank you very, very much indeed, for giving up your time. After all those things I told people that you're up to, it's amazing that you can give up 90 minutes to be with us this evening. I know you've got a case of traditional Liverpudlian refreshment under the table, ready to indulge in once we finish so we won't keep you any longer. But thanks again for your time. It's been really revealing, very informative. And I know everybody's very grateful for it.

Robert Moots
Thank you, Steven. A great pleasure and I hope it's been useful to your group. It sounds a really nice, engaged group, really good questions, and it's been great fun.