DIET AND THE IMMUNE SYSTEM

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Date?

Part 1

Good morning everybody, can everybody hear me? ('Yes!'). So today we're going to learn about diet and the immune system. Now, our immune system is absolutely essential for our survival, but it's influenced by a number of different things, including our diet, and the way that we live. So today I'm going to explain to you why nutrition affects your immune system, and also why this becomes increasingly important as we become older. I'm going to give you some examples of how specific nutrients in our diet affect the immune system, and at the end I hope to give you some highlights of some of the research that we're doing in this area.

So the immune system is a barrier to entry of pathogens. Pathogens are foreign bodies that we don't want inside us. So they include bacteria, viruses and parasites (things that would cause infections and that we want to keep out of our bodies). So the barrier is presented in several different forms: our skin first of all forms a barrier to the entry of those pathogens. The second barrier is our gastro-intestinal and respiratory tracts. So gastro-intestinal tract represents the tract that leads to your gut, and the respiratory tract is your breathing apparatus that leads to your lungs, and they also form a barrier that keeps out bacteria and viruses most of the time. We also produce mucus which has an important role in the immune system because it washes bacteria and viruses off the surfaces inside our bodies, and it stops them sticking and being able to get into our blood, because if they get into the blood, they cause an infection. So mucus is also very important. In our stomachs we produce acid. Now the acid in our stomachs helps us to digest food, but it also has a secondary function which is that it kills bacteria. It kills most of the bacteria that come in through our food – not all, but most. So it is important that our stomach produces acid to kill bacteria. And finally, we have some friendly bacteria in our gut, and I'll explain exactly what I mean by friendly bacteria and what they do,a bit later in the lecture.

Now of course, sometimes we do get infections. So obviously our immune system doesn't work a 100%, but if those pathogens, or bacteria, viruses, parasites, do get into our bodies, then our immune system has to be able to fight them. It has to be able to deal with them and remove them and destroy them. And the way that our immune system does this, is that it produces proteins that it releases into the blood, and those proteins recognise the foreign bodies. They coat them, so they stick to them, and that enables them to be recognised by cells of the immune system, and destroyed. So if those foreign bodies do get in to our body, then they can be destroyed by our immune system.

This is just a simple diagram to show you where the immune system is in your body. It's spread all over. So there are specific cells and tissues of the immune system that you find

all over your body. In your throat you have tonsils and you also have adenoids in the back of your nasal passage so they're shown here. You have a tissue called the thymus, which is in your chest. You have the spleen, which is in your abdomen. You have several collections of immune tissue in your gut, quite a lot of immune tissue in your gut. So you have the appendix, here. And also, there are lots of collections of immune tissue called Peyer's patches all the way through your gut. You also have lymph nodes, which you find in your throat or neck, in your armpits and also in the groin. So they're very rich in cells of the immune system. And your bone marrow is also a very important site for cells of the immune system. In fact, all of the cells of your immune system originally come from the bone marrow – that's where the're made. Once they've been made in the bone marrow they are released into your blood, so your blood is full of cells of the immune system. They're called white blood cells. And they can go from the blood into one of these other tissues where they mature. So when they're first produced from the bone marrow they are very immature. They are released into the blood, and they will go into the thymus or the spleen or the lymph nodes where they become more mature. In addition to those tissues, you also find, all of the time, that cells of the immune system are circulating in your blood, and also in your lymph, which is a type of milky liquid. In addition to that, cells of the immune system are scattered through every tissue in your body, and they have to be because they have to be everywhere looking for foreign bodies, looking for any bacteria or viruses that have infected you, so that they can deal with those. So all of the tissues of your body have cells of the immune system, but they're concentrated in these tissues.

Part 2

Now when you encounter a foreign body, whether it's a bacteria, a virus or a parasite, your immune system has to respond to it. And there are four very characteristic features of an immune response. The first is specificity. And what this means is that cells of your immune system recognise exactly what it is that is infecting you. So, for example, if you are infected by salmonella, your immune system will know exactly which type of salmonella is there, and it will respond to it in a very specific way. Likewise if you are infected with a very specific strain of flu, your immune system will know exactly which type of flu you are infected with, and it will respond to that. So our immune system is very sophisticated, very specific.

Now as you can imagine there are billions of different pathogens that could potentially infect us in our world. So what this means is that our immune system has to be very diverse. It has to be able to recognise millions of different types of foreign bodies that could potentially infect us. And people have estimated that our immune system can recognise about a billion different bacteria, viruses, parasites, and know exactly what they are.

Our immune system also, you might be surprised to discover, has memory. What this means is that if you encounter the same infection a second time, your immune system recognises it, and it will mount an even bigger response to that infection than it did the

first time. And this actually is the basis for vaccination or immunisation. In vaccination or immunisation you are injected with a foreign body – a type of bacteria or a type of virus. The virus is changed so that it won't actually give you an infection, so for example, its structure might be changed or it might be killed. It might be, you might be injected with a dead form of the virus. So that injection won't give you the disease itself, but what it will do, is it will expose your immune system to that foreign body, and your immune system will respond to it. What that means, is that if in real life you ever encounter that infection in reality, in a real situation, your immune system will already have seen that particular foreign body, and will be able to mount a big enough immune response to it, so that you don't get the infection because by vaccinating somebody you can train their immune system to recognise that particular bacteria or virus. That is what the vaccination is about. So memory is an important component of our immune system.

And finally, our immune system has mechanisms which allow it to self-regulate. What I mean by this is that the immune system has to know when to stop, and it does have signals which tell it to stop. It needs that because our immune system is very vigorous, and when it deals with something that's foreign, it destroys it by producing toxic chemicals which makes that foreign body explode basically, so it destroys it. But you can imagine that in the process of the immune system destroying something foreign, we might also suffer some damage to our own bodies. And in fact that is the case. So we have to make sure that the immune system, the damage caused by the immune system to our own bodies is limited, and that when the foreign invasion has been dealt with, that our immune system knows when to stop. So it has to be regulated. There are some situations where the self-regulation fails, and our immune system can't stop, and actually that's very harmful and I'll give you some examples of that a bit later on.

Now this shows you very clearly why our immune system is so important. This diagram shows the progress of a patient with HIV or AIDS. Now some of you might know that AIDS patients have to have blood tests very regularly, and during the course of those blood tests (which happen at least once a year) they have something done called CD4 counts. CD4 T cells are a type of cell of the immune system that you find in the blood. They are very important, and HIV patients have to have their CD4 T cells counted every year. In this patient, you can see that this time course follows over 12 years, and the numbers of their CD4 cells in their blood are shown in green. So you can see that over the course of time the number of CD4 T cells gradually becomes lower and lower. These cells are really important because they keep the HIV virus in check. They stop it growing too fast. They stop it dividing too much. So the number of HIV virus particles in the blood of this patient is shown in red. And you can see that for several years the number of HIV virus particles doesn't increase. It stays very low, and that's why people can live with the disease for a number of years.

But you can also see that when the number of CD4 T cells falls to a critical level, the number of HIV virus particles suddenly increases. And that is because this patient no longer has enough CD4 T cells to keep those HIV virus particles in check, and its growth, therefore increases. So you need cells of the immune system to keep the HIV virus in check. Once the number of those viruses starts to increase, you start to see the appearance of what we call 'opportunistic infections' here, and these are what lead to

death in an HIV patient. 'Opportunistic ' represents the fact that those foreign bodies (bacteria, viruses) see that the immune system is weakened, and they attack. And usually the types of infections that kill person with HIV or AIDS are flu and pneumonia, which of course are very common. Most people can overcome that, but in HIV patients they can't, because they don't have a strong enough immune system.

So there are several things that affect how well our immune system works. There are some things that we can't do anything about: our genetics, our gender, our age. But also our hormonal status, our previous exposure to pathogens, so the infections that we suffered in the past, and our vaccination history, can also affect how well our immune system works. But just look at the number of lifestyle factors that can affect your immune system. They include: stress, exercise, smoking, alcohol, possibly obesity, what is present in your gut, and diet and nutritional status. So this lecture today is going to focus on why diet affects your immune system, and how it does that.

Part 3

Now, we perhaps shouldn't be surprised that what we eat affects our health, because as long ago as the 5th century, the founder of medicine, Hippocrates, said "Let food be your medicine, and medicine be your food." But why exactly does your diet affect your immune system? Well, when you are challenged by a pathogen, so when something is trying to infect you, your immune system goes from a resting to an activated state. And activating your immune system requires energy. You need energy to fuel your immune system, and you need it for building blocks, and also for specific functions. So put very simply, when you have an infection, you need extra energy to fight the infection, but also you need specific nutrients because they have important functions.

There's a very strong interaction between nutrition and infection, and we've learnt this from developing countries where there is famine and poor nourishment. So if you're undernourished, it will lead to a weaker immune system, and it will make you more susceptible to infection with a pathogen. But the infection itself will lead you to become undernourished, and that means that you have a weaker immune system, and so on. So there is a vicious cycle between nutrition and infection, which is particularly a problem in developing countries. In the next slide I want to expand on that a little bit more.

So if we think about a situation where your immune system is activated because you have been exposed to something that causes an infection, the first thing that you need is more energy. So activation of the immune system means that you have an increased requirement for nutrients. But at the same time having an infection has a number of other effects: it decreases your appetite, it leads to poor absorption of nutrients, it might cause some damage to your intestine, and it might lead to diarrhoea. And all of those things together lead to a decrease in nutrient intake and absorption and an increase in nutrient losses. So, at exactly the same time that you actually need more nutrients to fight an infection, you are actually losing them and less able to absorb them efficiently. So this is a very critical situation and this is exactly why there is such a vicious cycle between nutrition and infection.

So there is no doubt that under-nutrition impairs immune function, and this encompasses under-nutrition in the form of a deficiency in both energy, and what we call 'macro-nutrients' - they are carbohydrate, protein, fat, the three key components of our diet. So if you're deficient in those it will impair immune function. But it also includes what we call 'micro-nutrients,' and that means vitamins and minerals. So those are things that don't actually give you energy but they're very important in many functions in the body. And normally you find that these occur in combination. So you could have a deficiency in energy, carbohydrate, protein, fat and also vitamins and minerals. As I've said, this is a particularly important issue for developing countries, especially in times of food shortage and famine, natural disasters, the flooding in Pakistan is very relevant here, poor soils, poor living conditions, and limited access to health services. But actually there are also vulnerable groups in very developed countries, particularly the elderly, babies who are born too early, patients in hospital, and patients with cancer. So it's a relevant problem in both developing and developed countries.

Part 4

This is a really good illustration of the severity of the impact of malnutrition on immunity. This is data from a study that was carried out in Bangladeshi children, and it shows you the number of episodes of diarrhoea, in these two bars here, and the duration of episodes of diarrhoea, in these two bars here. And what we're comparing here is well-nourished children with malnourished children. So the well-nourished children are shown here in the purple, and the malnourished children here shown in the pink. And what you can see here is that the malnourished children have a higher number of episodes of diarrhoea than those that were well-nourished, and a very significantly higher duration of episodes of diarrhoea compared with the children that are well-nourished. So malnourished children have more severe diarrhoea than those who are well-nourished. This is really important because diarrhoea is a major factor in childhood death in developing countries. So being poorly nourished is directly linked to a higher rate of mortality, a higher rate of death, in developing countries, particularly when you look at the link between malnutrition and diarrhoea.

I'm going to look at some specific nutrients now to show you exactly how they affect the immune system, and what is the evidence that they affect the immune system? I'm going to focus on micro-nutrients, that is, vitamins and minerals, and I'm going to show you examples of two vitamins and two minerals that have been shown very clearly to affect the immune system. But before I do that I just want to introduce some general concepts about the effects of vitamins and minerals on the immune system.

The first concept is that a deficiency in vitamins and minerals can very quickly lead to an alteration in immune response, and the extent of the impairment of the immune response depends on how severe the deficiency is, whether the person already has an infection, and what their age is, how old they are, because in older people deficiency can have a bigger impact. It's also really important to understand that for many micro-

nutrients, excessive intake, that is taking too much, is also associated with impaired immune response. There is often a tendency to think that just because something is good that taking more is better. That is definitely not the case. And in fact we have very good evidence to suggest that if you take too much you can actually do a lot of harm, and I'll give you some specific examples of that in a few minutes.

So I want to start by looking at vitamin A, as my first example. Vitamin A is what we call a fat soluble vitamin. We actually don't need very much. And in most countries, people have very adequate intakes of vitamin A. You don't even need to eat it every day, because our bodies store it very well. You find it in dairy products, so milk, cheese, yogurt. You also find it in eggs and also quite high quantities in oily fish like mackerel, salmon and so on. But there are places where there are deficiencies in vitamin A, and it's been shown that deficiency in Vitamin A is associated with increased risk of infection. Vitamin A is particularly important in maintaining the structure of our gut, and our gut you remember is one of the physical barriers of the immune system. And it's also really important in skin function, so it maintains the healthy skin. So if you are deficient in vitamin A, it's associated with the breakdown of the integrity or the structure of the gut. Your gut becomes weaker and more leaky, so infections are more likely to penetrate into the gut. And it's also associated with skin function- with skin infection, because skin function is not as good if you are deficient in vitamin A.

Now a lot of studies have been done in developing countries where people who are deficient, especially children, who are deficient in vitamin A, are given supplements of vitamin A, and the effects are recorded. So it's been shown in a lot of studies that replenishing vitamin A in people who are deficient decreases mortality, decreases death in children age 6 months to 5 years by 30 percent. And it's also been shown that frequent small doses are better than infrequent high doses. So it's better to have small amounts frequently, than to have large amounts, but not very often. It's been shown in those studies that giving vitamin A to people who are deficient regenerates their damaged gut tissue and it reduces the incidence and duration of diarrhoea. As I said that's very important because diarrhoea is a major factor in childhood death, especially in this sort of age, under the age of 5.

So there's a strong relationship between vitamin A and gut infections particularly, also skin infections. There is also some interest in vitamin A and respiratory infections. So things like cold and flu. But the evidence in that area is much more contradictory. And it seems that the effects of vitamin A very much depend on whether the people are well nourished or malnourished in the first place. So it's been shown that in malnourished children, low dose supplements of vitamin A can reduce the severity of infection. But that's not seen in children who are not malnourished. And in fact, in children who are not malnourished, some studies have shown that vitamin A actually increases the severity of respiratory infections. This is a good example of where if someone already has enough of a particular nutrient, then giving more is not necessarily a good thing, and in fact, it can actually be harmful. So if you have children who are deficient in vitamin A, they can benefit from having supplements in terms of respiratory infections. But if you give vitamin A to children who are not deficient, then it can actually cause harm.

So why should Vitamin A cause harm in children who are not malnourished? Well we think it's because vitamin A encourages production of mucus, and normally that's a good thing. But if you have too much mucus, and you get a respiratory infection, then actually that can make your infection more severe because you can't clear all that mucus, and so in situations where people already have enough vitamin A, but they get more, and they produce too much mucus, that can actually make their infection more severe. So there are good reasons why you need to look at whether somebody is already deficient, and only use supplements if they are deficient in the first place.

Part 5

So my second example of a vitamin which affects immune function is vitamin C. And we find vitamin C in a wide range of fruits and vegetables. As I said vitamin A is fat soluble, vitamin C is water soluble. So our bodies actually don't store it very well. And we do need to have a frequent intake. We need to take vitamin C in every day. There's been a lot of discussion about whether vitamin C can influence respiratory infections in particular. So most of the research that has been done has been looking at whether vitamin C affects colds and flu. Now there does seem to be some modest benefit of vitamin C supplementation on the duration, but not the incidence of respiratory infections. So what that means is vitamin C doesn't prevent you from getting a cold or flu, but it can decrease the severity slightly if you do get one. Now the size of the effect is modest. It's actually very small. So in adults, the size of the effect is about 8 percent. So to put that in real terms, if you took Vitamin C, you would feel about 8 percent less bad than if you didn't. It's quite a small affect. In children the effect is about 14 percent. But the important thing to realise is that you actually have to be taking Vitamin C before you get the infection in order for it to have even that small benefit. If you take it afterwards it's too late. So you have to be taking Vitamin C before you get the infection to have a small effect on the severity of the infection.

Now this is the conclusion on studies in people who are generally healthy and living in good conditions. But if you look at people who live in very crowded conditions, or people who do a lot of strenuous physical activity, then there actually is some additional benefit. So studies have shown that the incidence of common colds and pneumonia can be reduced by vitamin C in people who do strenuous physical activity, or who live in crowded conditions. So those people who are particularly vulnerable could have a lower incidence of colds and pneumonia if they take vitamin C. So again you can see that there is a split between people depending on their situation. If you are generally well and well nourished you don't get that much benefit from vitamin C, but if you are living in crowded conditions and you are particularly vulnerable, then you do get some benefit. It's the same when you compare well nourished with malnourished children and the situation with vitamin A. So if there is nothing wrong with you, you probably don't need any extra help. But if you are in a particularly vulnerable group, then vitamin C might be a benefit. So as I said most of the research on vitamin C has been done in respiratory infection. There is really not very much information about other types of infections.

So I am now going to look at two minerals. The first one I am going to look at is zinc. You find zinc in meat, in dairy products, in shell fish, and also in bread and cereals. And a deficiency in zinc is associated with increased susceptibility to infection and increased risk of mortality. Zinc has an especial impact on the bone marrow, and also on what we call lymphoid organs. So that includes the lymph nodes, the thymus and the spleen, all of those important tissues in the immune system that I showed you at the beginning. The fact that it has an important impact on the bone marrow is notable, because as I said at the beginning, the bone marrow is where the cells of the immune system are originally made. And so if a deficiency of zinc is present, then your bone marrow is less able to make cells of the immune system. You have smaller numbers in the blood. You have smaller numbers in your tissues. You are less able to fight an infection. It's also been shown that low levels of zinc in your blood can actually be used to predict your risk of infection, and diarrhoea, especially in malnourished populations.

So I'm going to show you some examples of two studies that were carried out on zinc and immune function in children. The first one looked at malnourished children who were given supplements of zinc orally, - so they were given tablets containing zinc, - and the size of their thymus was measured before and after they were given the zinc tablets. And they were given zinc tablets for ten days. So the thymus, if you remember, is one of the tissues of the immune system that you find in your chest. And it's a very important organ where cells of the immune system mature. And you can see here that in almost every child the size of the thymus increased very significantly after the zinc treatment. You can see that deficiency in zinc has a marked impact on those tissues, and giving zinc improves the size and the functions of those tissues very significantly.

On the right hand side here is an even more interesting experiment. This involves what we call the skin-prick test, and this is where you prick the skin with something that sensitises the immune system. You deliver it just under the skin with a needle. Your immune response takes about 48 hours to develop, and after 48 hours you see a little red bump. It's very similar to allergy testing. And you can actually measure the effectiveness of your immune system by doing a skin-prick test, because the bigger the bump, the better your immune system, the better your immune response, the stronger your immune system. So in this study on the right side, malnourished children were given two skin-prick tests, one on each arm. On one arm, they were given no extra treatment. On the other arm, they were given some zinc ointment which was rubbed on to the skin at the same time as their skin-prick test. And what you see here is the size of the bump after the control treatment, and the zinc treatment in each of the ten children. So you can see that in almost every case, the site where the zinc was applied, produced a significantly bigger immune response than the control size. So this shows that applying zinc to that test improves the immune response.

It's been shown in a number of studies that zinc supplements decrease the incidence, the duration and severity of childhood diarrhoea. So again important because diarrhoea is a major component in childhood mortality. But, again I would emphasise that just because something has a beneficial effect it doesn't mean that more is better. And it's been shown very clearly that if you take too much zinc, very high intakes can result in the depletion of copper from your body. And copper deficiency can actually impair your

immune system. So taking too much zinc can be harmful for a number of reasons, but also because that too can impair your immune function.

Part 6

My last example is another mineral called selenium. And I've chosen this one because at the moment many populations are thought to have marginal dietary deficiencies of selenium. This includes much of Northern Europe, Russia, New Zealand and some parts of China. And the reason for that is that one of the major sources of selenium in our diet is from bread and cereals but the soils in a lot of these places are quite poor in selenium. So if you grow grains and cereal in soil that's poor in selenium, then the grains themselves will be poor in selenium. So what you eat is not as selenium- rich as it could be. So the other sources of selenium are Brazil nuts. They are very rich in selenium. Different types of fish, eggs and meat, but as I said bread and cereal are important sources of selenium. And some of our bread and cereal is actually quite poor in selenium at the moment. The current intakes of selenium in the UK are between 29 and 39 micrograms per day. The recommended nutrient intake is 75 for men and 60 for women. So in the UK, we are eating about half the amount of selenium that we should be. The upper safe limit is very high at 450 micrograms per day.

Now the research on selenium is still at quite an early stage. So we still don't know very much about the impact of selenium. But one study was done in the UK a few years ago. And this was a study that was done specifically in people who were selected because they were selenium-deficient. And they were given supplements or tablets which contained either 50 or 100 micrograms per day of selenium, or a placebo (which is a dummy treatment). And 6 weeks after they were started on the supplement, they were given a single dose of the polio vaccine, and the purpose of that was to test how strong their immune response was. The study showed that in those people who were selenium-deficient, giving them supplements increased the number of their CD4 cells. Those are the cells I showed you at the beginning that are important in keeping the HIV virus in check and actually most bacteria and viruses. And also giving selenium brought about an earlier response to the polio vaccine. So there are some evidence indicating that selenium could be useful in improving the immune function, but it's still at quite an early stage.

Now of course when you buy supplement of vitamins and minerals, you don't buy them individually. You usually buy a multivitamin and mineral mix. So an important question is if you take those combinations, if you take the multiple vitamins and minerals, does it have any effect on your immune system? Well we think that it might be of benefit to athletes because studies in athletes do show some benefit. But in studies in older people, those combinations don't seem to protect against infection. And we think that the reason for that is that the doses of individual vitamins and minerals, when you have a mixture, are too low to provide enough of a benefit. There is a problem with some of the research in that area because there is a lack of consistent methodology, and also study design. So we see this as an important area for future research, because there are still a

lot of questions about the potential benefit from taking multiple vitamins and minerals. There's also not very much information on what combinations of micro nutrients do in children, or in populations from developing countries, because most of those studies so far have been done on single nutrients.

Part 7

Now I said that I was going to explain why the effects of the immune system, nutrition on the immune system become increasingly important as we get older. The population worldwide is getting older. It's estimated that by the year 2050, 21 % of us is going to be classed as elderly. So it's important to us to try to maintain our health for as long as possible. But it's also true that our immune function declines with age and poor immune function is associated with high mortality.

Now influenza or flu is a very important disease when considering ageing, because those individuals aged over 65 account for more than 90 % of deaths from flu, and they're more likely to develop complications such as pneumonia following an infection. In the UK people aged over 65 are entitled to free flu vaccination every year in October and November which marks the start of our flu season. But it seems that whereas young people respond very well to flu vaccination- they have a good strong immune response to flu vaccination- older people don't respond as well, and it's thought that while younger people the efficiency of flu vaccination is between 70 and 90%, in older people it's as low as 17 to 53%. So more than half of older people who get the flu vaccination actually don't respond to it, and are not protected simply because their immune system is not strong enough to respond to the vaccination. So it's a waste of money, and it leaves them very vulnerable.

They're the same people who are most at risk of nutritional deficiencies, so older people are at risk of deficiencies in all of these nutrients. So you can see now why the older age group, elderly people, are particularly at risk of this interaction between nutrition and immune function.

Now that's not the end of the bad news about getting older, because as you get older, the degree of inflammation in your bodies also increases. So when I talk about inflammation, I'm talking about redness, swelling, heat, pain, the things that you identify with swollen joints. All of that increases as we get older. Inflammation is brought about by a group of proteins that are produced by the immune system that are called cytokines. And TNF, or Tumor Necrosis Factor, is an example of one cytokine, there aren't very many. But it's been shown that older people have about double the level of inflammatory cytokines than younger people. And if you look at this graph on the right hand side you see that with increasing age you see an increase in the level of TNF in the blood.

Now TNF and other inflammatory cytokines have a number of undesirable affect so they include inflammation, loss of lean body mass, that's loss of muscle, loss of bone, they are associated with dementia, they are associated with insulin resistance and diabetes, and

they are associated with a poor outcome from injury, surgery and trauma. So this increasing inflammation that we suffer as we get older, is not a good thing. In addition, too much inflammation by the immune system is associated with the number of diseases. And they include arthritis, inflammatory bowel disease, psoriasis, asthma. In fact these diseases don't just affect older people, they also affect younger people. And they're a good example of where the immune system fails to self-regulate. The immune system in these cases, in these diseases, does not know when to stop, so it becomes overactive and actually leads to disease.

Part 8

I'm going to just show you a few slides that are specific to rheumatoid arthritis to show you what one of these diseases is like, and whether there is anything that diet can do to improve the situation in someone who had a disease like this. So rheumatoid arthritis has no cure. It's called an auto immune disease, because the immune system in people who have this attack the joints when it's not supposed to. So it's characterised by infiltration of cells of the immune system into the joints where they shouldn't be. And those cells are inflammatory and they cause destruction of bone and cartilage. And you also, in patients who have rheumatoid arthritis, see the appearance of inflammatory cytokines like TNF in the blood. This is just a very simple diagram to show you the difference between ordinary arthritis and rheumatoid arthritis. So ordinary arthritis, which happens to a lot of people as you get older is caused by the cartilage at the end of your bones gradually wearing out so that the bones start rubbing together, and that's very painful. In rheumatoid arthritis, it's not caused by the bones rubbing together. It's caused by cells of the immune system entering from the blood, into the joint capsule, and causing inflammation that's shown by red here in the joints. And that can have the secondary effect of causing bone erosion. But you can see that's not caused by the bones rubbing together. It's caused by the immune system entering the joints when those cells shouldn't be there.

So is there anything that diet can do to help patient with rheumatoid arthritis when there's no cure; the only option for those patients is to take very high dose anti-inflammatory drugs which have a lot of side effects. It's not very pleasant. And it does seem from some of our research that fish oil could be beneficial because fish oil contains omega-3 fatty acids that are thought to have anti-inflammatory effects. There's strong evidence of effects in humans of fish oil fat on blood fats, on coagulation, on inflammation and also on heart disease. So you find these omega-3 fat in fish oil capsules and also in oily fish.

Now the evidence, in terms of rheumatoid arthritis, comes from clinical trials. And there've been at least 17 of those trials to date. 16 out of 17 of those trials report an improvement in clinical outcome. And some of them show quite dramatic improvements. Some of the studies also show that patients who take fish oil are less reliant on their anti-inflammatory drugs than patients who don't take fish oil. So there is quite good evidence accumulating that fish oil could be beneficial in patients with rheumatoid arthritis. We don't know whether that's the case for other types of inflammatory diseases.

But some rheumatologists have therefore concluded that the findings of benefit from fish oil are quite robust, they ask why don't people use fish oil supplement more widely in rheumatoid arthritis, and they suggest that dietary fish oil should be regarded as a part of the standard therapy for a disease which has no cure.

Part 9

Now in the very last few minutes I'm going to talk about the other area of research that we're interested in, and that is probiotics. Now has anyone here heard of probiotics? Put your hand up if you have heard of probiotics. A few people. OK. So let me explain what probiotics are. Probiotics are live bacteria that you find in many types of fermented foods. So you probably actually have heard about them but didn't realise. So they're found in a lot of fermented milk drinks, they're found in live yogurts, they can be bought in capsules. They are live bacteria that we consume and those bacteria, if they survive, are thought to have beneficial effects in our guts. So they're promoted mainly for the digestive health. But in addition, more recently, they've been promoted to enhance the immune function and to curb inflammation. So let's just have a quick look at probiotics and look at whether they really do affect immune function.

So probiotics have a long and safe record of use in humans. They are well established benefits for mild gut disorders. So they're supposed to improve constipation, diarrhoea, general gut function. But in addition, they're suggested to modulate immune function. Now if we think about the ways that probiotics work, in all of our guts we have billions of bacteria and people have very simply divided these into good bacteria and bad bacteria, or unfriendly bacteria and friendly bacteria. The bad ones are the ones shown in red here and the reason that they're bad is that they create nasty gases, they are putrefying, they produce nasty chemicals, and they cause diarrhoea and infections. So these are not good. The ones that are good are shown in green, and they're good because they inhibit the growth of the bad ones. They are thought to help your digestion and absorption. They're thought to stimulate your immune function. And they help make vitamins. So there are two classes of bacteria that are all good, and they are lactobacilli and bifidobacteria. These are the ones that you find in live yogurt and fermented drinks. You can see that there are also some bacteria in our gut that are both good and bad. So the good ones, the ones that we add to our probiotics are these two: lactobacilli and bifidobacteria. And the thought is that if you eat these probiotics in your foods, and they survive your stomach and get into your gut, then they can colonise in your gut and they can balance out the bad bacteria. So this is why we call them friendly bacteria because they help to maintain a balance between the good and bad bacteria in your gut. And in addition, we think that they might stimulate immune function.

Now the reason for the link between the gut and immune function is as I showed you at the beginning, our gut is actually a very rich source of immune tissue. In fact some people think that as much as 70 percent of your immune system is in your gut. So there could be a direct affect of probiotics in the gut which influences our immune system. It's been shown in children that probiotics improve recovery from rotavirus and non-bloody diarrhoea. They decrease the incidence and severity of diarrhoea in day care centres, and they decrease the duration of diarrhoea in hospital. Also the duration of antibiotic-

induced diarrhoea. In adults probiotics are thought to decrease the incidence of travellers' diarrhoea. That's only been shown in some studies.

So the idea that has been put forward recently, is that some probiotics might improve the response to vaccination, and some studies have shown that some probiotics improve the response to flu vaccination and to polio. So this could obviously be very useful in those older people who don't have a very strong immune system but take, but have the flu vaccination every year and are not responding to it effectively enough. If there is something that they can consume in their diet that would improve their response to the flu vaccination, then that could be beneficial. And we're doing a very large study at the moment to look at exactly that. We are looking at the effect of a specific probiotic on the response to flu vaccination in people aged over 65.

OK. So I'm going to finish now just by summarising the main points that I covered in this lecture today. I hope I've shown that there is a strong relationship between nutrition and immune function, that there are specific examples of nutritional deficiencies which impair immune function, and the studies that show that supplementation can restore it; that there are risks associated with taking excessive nutrient; that as we get older our immune system declines and we are more at risk of nutritional deficiencies. There's evidence that fish oil could be useful in inflammatory conditions. So far the research has been mainly focusing on rheumatoid arthritis. And finally, that there's growing interest in the potential for probiotics to enhance our immune system. So I'd like to thank you for your attention, and hopefully there'll be time for me to answer a few questions if you have any. Thank you.