#278: Stuff the staff: Understanding and treating celiac disease

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

SHANE HUNTINGTON
I'm Dr Shane Huntington. Thanks for joining us. For people with coeliac disease, consuming foods that contain gluten can be a severe health hazard and that hazard is all too pervasive. Inspect the ingredients lists of many foods on the supermarket shelf and you will easily note the presence or potential presence of gluten. To make matters worse, coeliac disease is being diagnosed more and more frequently. As awareness of coeliac disease has increased, supermarkets are cashing in on people seeking a gluten free diet. Many supermarkets now have significant sections dedicated to gluten free products, but are coeliac sufferers forever doomed to modify their diets? Will there ever be treatments for the condition, and what directions are researchers in coeliac disease taking? Today on Up Close we speak with a clinician researcher who is an expert not only on the diagnosis of coeliac disease, but also on the research towards potential vaccines and other treatments for this lifestyle altering condition. Dr Jason Tye-Din is a gastroenterologist and head of coeliac research at the Walter and Eliza Hall Institute here in Melbourne. Welcome to Up Close, Jason.

JASON TYE-DIN
Thanks very much for having me.

SHANE HUNTINGTON
Jason, as a gastroenterologist, how do people that you see present when they actually have coeliac disease? What sort of things do they come in with?

JASON TYE-DIN
So coeliac disease can present with a variety of different symptoms, I would typically see patients who complain of irritable bowel type symptoms. So that include bloating, abdominal pain, altered bowel habits such as diarrhoea or constipation and many people had already been diagnosed with irritable bowel or misdiagnosed. Chronic fatigue and lethargy is another common symptom and often nutrient deficiencies such as low iron or iron deficiency anaemia. So these are common
presentations, but we do recognise that there are a whole broad variety of other manifestations of coeliac disease.

SHANE HUNTINGTON
Now, once you’ve identified these particular symptoms that a patient has come in with, how do you go about diagnosing them, specifically with coeliac and not something like IBS as you mentioned?

JASON TYE-DIN
So coeliac disease is a result of an immune response to gluten in the diet and it happens in genetically susceptible people. And so what we do nowadays is to screen for coeliac disease using a blood test that measures antibodies that are elevated in the blood of people with coeliac disease. If that is elevated then that’s a sign that that person is likely to have the condition. And then we go on to demonstrate what we call the gold standard diagnostic which is the damage in the small bowel and we undertake a gastroscopy which allows us to take small bowel biopsies and show that characteristic damage and that will confirm a diagnosis of coeliac disease.

SHANE HUNTINGTON
Jason, when you speak about damage to the small bowel, what exactly do you mean?

JASON TYE-DIN
So the appearance of the small bowel in coeliac disease under the microscope is quite different from a normal healthy bowel and we actually see is the villi, normal finger like projections of the bowel which help increase the surface area for absorption of nutrients is completely damaged and inflamed and eroded. So there’s in effect a flattening of the lining of the small bowel. And what we actually see is a dramatic reduction in the surface area for absorption of nutrients in the bowel and in fact this falls from the size of the normal bowel which is about the size of a tennis court if it was all laid out flat to about the size of just slightly larger than an A4 sheet of paper, so this can account for the dramatic problem with nutrient deficiencies in coeliac disease. But that’s one part of the equation and the other part as I’ve mentioned is that there is persistent inflammation which also contributes to problems around the body.

SHANE HUNTINGTON
In addition to the first blood test you talked about I understand there’s also a genetic test that can be done as well. What happens when a person comes back with a negative in that genetic test for the particular coeliac genes?

JASON TYE-DIN
That’s right, so we now understand and this is research which has only probably been out for about 20 years or so that there’s a very strong genetic link in coeliac disease. In fact almost 100 per cent of people with coeliac possess two varieties of a HLA gene called HLA-DQ2 or DQ8. The HLA genes are very important in the immune system function. HLA stands for human leukocyte antigen. What they
actually do is code for molecules that sit on the surface of immune cells and tell the immune system what to recognise. And in the case of coeliac disease the HLA-DQ2 and the DQ8 genes encode these molecules that actually can recognise gluten. But the remarkable thing about this gene test that can be done nowadays is that if a person doesn't have either DQ2 or DQ8 we can be very confident that coeliac disease is not likely to be present in that person. So as part of the toolkit if you like that doctors use to help diagnose coeliac disease the gene test can be useful in very select cases, particularly when the result is negative to help exclude a diagnosis.

SHANE HUNTINGTON
Coeliac is something that few would have heard about, even just a few years ago. It seems to be on the rise. But it now seems quite common. Has something changed, or are we just diagnosing it more often because we're better at doing that?

JASON TYE-DIN
The answer is a bit of both. The evidence suggests that coeliac disease is actually becoming more common and if you look at studies from Finland or the United States there has been approximately a doubling of coeliac disease every two decades and in the last 50 years the prevalence of coeliac disease has increased fourfold. So there's no doubt that the condition is becoming much more common, but the actual drivers for that, why that's happening, isn't well understood. But on top of that there's no doubt that there's increased community in medical awareness of coeliac disease so increased testing is detecting more cases of coeliac and that's contributing to the rise we are seeing as well.

SHANE HUNTINGTON
When you mentioned the genetic test, what sort of percentage of the population actually has the genes that would lead to coeliac disease potentially?

JASON TYE-DIN
The two genes that I mentioned, the DQ2 and the DQ8, most of the literature quoted about 30 to 40 per cent of the general population as having that and in fact in Australia we've conducted a recent study that shows 56 per cent of the Australian population possess DQ2 or DQ8. Now, that's not the whole story. We know that other genes are probably relevant in leading to the development of coeliac disease. And we also know that there are environmental factors that are important in triggering coeliac disease. So I think that at the end of the day we are dealing with the condition that has a genetic basis, but there are other factors such as environmental and the presence of gluten in the diet that determine whether it manifests and develops or not.

SHANE HUNTINGTON
You mentioned in Australia the statistics are in excess of 50 per cent of people having the gene for coeliac disease. How does this play with hereditary? It is a requirement that both parents would have the gene or is one parent enough, or can we just randomly end up with this mutation?
JASON TYE-DIN
So we know that coeliac disease relies on multiple genes that predispose to the condition as well as those environmental factors. So the HLA-DQ2 and DQ8 genes are part of the picture and they seem essential for the development of the condition, but not enough on its own. So compared to some genetic conditions like let's say cystic fibrosis where if you have the gene you are going to have the condition that's not the case in coeliac disease. And so the vast majority of Australians who have HLA-DQ2 or DQ8 will not develop coeliac disease. What we do see is that there's a 10 per cent prevalence of coeliac disease in someone who has a first degree relative with the condition. So there's certainly a hereditary or genetic component and if there's a family history of the condition we always view those people as being more likely to have the condition.

SHANE HUNTINGTON
Now people come out with coeliac disease at a variety of times in their life. There doesn't seem to be a specific age dependence. Are you seeing some particular things that are saying, okay you get exposed to this or you do this and you end up with the disease because you've got the gene?

JASON TYE-DIN
It's a very good point. We can see coeliac disease occurring any time from infancy when a child is weaned onto gluten in the diet right through to old age. I've got some patients who are 90 plus years of age who have been diagnosed. And so in many of those cases the coeliac disease occurred later in life, but in some of those cases the coeliac disease occurred in early infancy but wasn't diagnosed until later in life. And what triggers the development is still not well understood. There are epidemiologic studies that often link various environmental factors to the development of coeliac disease. For instance recurrent gut infections such as rotavirus may increase the risk of coeliac disease and conversely breastfeeding at the time of introducing gluten into a baby's diet may be protective against the development of coeliac disease. The bottom line is that there appears to be these environmental triggers, but they're not well described.

SHANE HUNTINGTON
Jason, when we look around the world how common is coeliac disease, and is it one of these things similar to type 2 diabetes for example that we find more prominently on Western diets?

JASON TYE-DIN
Traditionally we used to think coeliac disease was more common in people of Celtic origin, but now we know that coeliac disease is very widely found around the world and in fact the highest prevalence of coeliac disease is actually seen in Northern Africa in an area near Algeria. There's a tribe of people called the Saharawi who have about six per cent prevalence of coeliac disease. The genetics for coeliac disease relate to a Central Asian gene, so it's common all around the world and typically we see about a one in 100 prevalence for coeliac disease in Europe, North America and in Australia, one in 70 people have been shown to have coeliac
disease. And it's now an emerging condition in some of the Asian countries. For instance in China there are some publications coming out now that coeliac disease is being found and that's particularly the case for those people who are adopting a Western type diet richer in gluten.

SHANE HUNTINGTON
We've discussed this somewhat before you and I because my wife has coeliac disease and we talked about the possibility of pregnancy being a trigger in some women. Is there any data to correlate that, or is it just something you sort of observe at the moment in population sets?

JASON TYE-DIN
It's largely anecdotal, but in my practice there are many patients that I see who swear that after they had their first or second child that coeliac disease symptoms began. And there is evidence to suggest that hormonal changes can be triggers in the genesis of some immunological diseases. So there is a biological basis for that observation.

SHANE HUNTINGTON
I'm Shane Huntington and you're listening to Up Close. Today we are speaking about coeliac disease with clinician researcher, Dr Jason Tye-Din. Jason, in terms of gluten which is I guess the heart of the problem here, what is gluten, and what is it about gluten that is problematic for the body of someone with coeliac disease?

JASON TYE-DIN
Gluten is a storage protein that's important for the germinating grain. And it's found in primarily wheat, but also rye, barley and to a lesser extent oats. It's the gluten protein that is toxic to people with coeliac disease. We know that there are certain fragments of gluten that appear to drive that abnormal immune response seen in coeliac disease and this links in very nicely to the immunological and the genetic predisposition that people have who have coeliac disease.

SHANE HUNTINGTON
How do you go about determining that? How do you go about pulling out what aspects of these various compounds are problematic? I mean you?ve done this yourself in your lab.

JASON TYE-DIN
That's right and this has been the holy grail of immunologic research, identifying what drives immune diseases. When I talk about autoimmune disease, I'm referring to conditions such as type 1 diabetes or multiple sclerosis or rheumatoid arthritis and in those conditions we understand that there are certain organs within the body that are attacked by the immune system. The actual components of those organs that are driving that immune response remain very poorly defined. So for instance in type 1 diabetes we know that the Islets of Langerhans in the pancreas are attacked, but the actual fragments of the protein, the peptides driving that haven't been well understood. In our case for coeliac disease we know that gluten drives that immune
response, but the actual gluten peptides causing coeliac disease up until relatively recently weren't well understood. So that's been the basis of my research to try to find out how to approach that.

SHANE HUNTINGTON
Jason, let's go on a bit of a tour of the digestive system if you like? When the gluten heads into the digestive system what is happening, and at what point does that immune response occur? What's the effect on the surrounding areas of that response?

JASON TYE-DIN
What we understand is that there are a number of stages to the development of coeliac disease. Gluten is a peculiar and quite unique protein. It's a very complicated protein as well, so it's made up of thousands and thousands of different peptides and they vary depending on whether it's from wheat, rye or barley or oats. We know that one of the common properties of the toxic parts of gluten is that it contains a lot of an amino acid called proline and proline imparts resistance to digestion by the typical digestive enzymes, the proteases that typically break down proteins. So what we observe is that the toxic parts of gluten actually survive digestion in the body and they are able to actually pass across the gut lining and come into contact with the immune system. The next step is that there are enzymes in the gut lining called transglutaminase and this is an enzyme that actually modifies gluten to make it become more toxic to the immune system. What happens after this modification is that the modified gluten peptides combine to immune cells called antigen presenting cells and if those antigen presenting cells carry molecules encoded by the DQ2 or DQ8 gene then there's a subsequent adverse immune response which leads to the damage typical of coeliac disease. So it's a sequence of events that starts with gluten in the gut lining being modified and then binding with the immune system and the reaction occurring in those people who have the appropriate genetic markers.

SHANE HUNTINGTON
So not only is our system missing the toxic part of what we are consuming there, it's making it more toxic.

JASON TYE-DIN
That's exactly right. So we're not breaking down the toxicity and for people with coeliac disease those gluten peptides become more toxic, they bind to the immune system and then it triggers this cascade of events which ultimately lead to the damage typical of coeliac disease in the bowel, but also the other organs, the skins, the brain, the bones, the liver.

SHANE HUNTINGTON
We've in previous episodes of Up Close talked a lot about allergies. This is very different. Can you describe the difference between a food allergy and an autoimmune response like the one that we get when we consume gluten?
JASON TYE-DIN
That's exactly right and I think sometimes coeliac disease is mistakenly considered a gluten or a wheat allergy and it certainly is not that. An allergic process involves different parts of the immune system. It can be antibody driven and this is an antibody called IGE and sometimes there are other mechanisms that are non-IEG mediated. However, in coeliac disease and other autoimmune diseases T-cells can be the driving factor, so that's another part of the immune system and in coeliac disease T-cells that are specific for these gluten peptides that really are fundamental for the development of the condition. So we don't see anaphylaxis to gluten in coeliac disease. We don't see allergy symptoms such as hives or itchy mouth or throat swelling. We see a completely different spectrum of effects related to gluten in coeliac disease.

SHANE HUNTINGTON
Presumably that completely changes your approach to finding a way around this too. Because one of the things that is being done more and more especially in children to negate the issues of allergies is for them to be exposed to small extents when they are very young. With coeliac disease presumably this would be the worst possible thing you could do.

JASON TYE-DIN
Well, actually the interesting thing now is the emerging evidence suggests that we can probably borrow a lot from the allergy world and there is at least one study from the United States that suggests there is a window period that exists between the ages of four to six months in infants where the introduction of gluten is probably optimal for the development of tolerance to gluten. So there are some recommendations now that suggest that mothers should introduce small amounts of gluten to their child at around four to six months, ideally while breastfeeding in order to reduce the chances of their child developing coeliac disease. So there are some recommendations now that suggest that mothers should introduce small amounts of gluten to their child at around four to six months, ideally while breastfeeding in order to reduce the chances of their child developing coeliac disease. So it's an intriguing area which we really need some better quality studies to give us the right answers, but there certainly appears to be the development of immune tolerance to gluten occurring at quite an early age in childhood, similar to some of the allergy kind of work that is occurring, for instance such as a peanut allergy.

SHANE HUNTINGTON
Presumably this would not be effective in adults who are on a gluten free diet, to slowly reintroduce gluten into their diet would be problematic?

JASON TYE-DIN
What we do see is that when people with coeliac disease who reintroduce gluten into their diet there's unfortunately damage occurs back in the small bowel. Symptoms often recur. It's not a durable long term intervention. It's interesting though that patients often find the symptoms can ameliorate after the first day or so, but unfortunately it's really the bowel damage that we worry about in coeliac disease and most of the long term medical studies show that the complications of coeliac disease such as osteoporosis or certain malignancies such as lymphoma correlate very strongly with persistent inflammation in the small bowel. So we really advise patients against consuming gluten when they have coeliac disease because of the risk of
those complications.

SHANE HUNTINGTON
I want to talk a bit about those complications, the difficulties that the patient would experience. Obviously when you discover that you have coeliac disease and some people may have been living with it for some time, there is a degree of damage in the gut, but there are a whole lot of secondary effects. Can you speak to what some of those effects are, and how the repair process actually works in the gut and in those secondary areas as well?

JASON TYE-DIN
Right, in the 1950s gluten was identified as the driver of coeliac disease and back then it was really considered a gut disease, a condition that really affected the bowel and caused problems with absorption of nutrients and weight loss and diarrhoea, but in the last 50 years we've really appreciated that coeliac disease is more than a gut condition. In fact we classify it now as a systemic immune disease. By that we mean that there are multiple organs affected, liver, bone, brain, joints, skin, et cetera. So we understand that the immune response to gluten occurs in the bowel. It targets the bowel, but it's not restricted to the bowel and that many organs can be affected. So when a person is diagnosed and treated and they go gluten free that driver for that abnormal immune response is removed and that we typically see over about 12 to 24 months healing of the small bowel and it can return completely to normal which is fantastic. We also see an improvement in the other organs, whether it's the skin affected or the liver for instance. So the effects can be wide ranging, but in some cases, particularly when coeliac disease is diagnosed later in life the effects and the damage that's occurred has already occurred to such an extent that not everything is fully reversible by a gluten free diet.

SHANE HUNTINGTON
When we talk about those secondary effects is that a result of the immune system itself there, or is it a retraction of the nutrients that are being absorbed by the body and we're essentially starving those parts of the body that's causing the problem?

JASON TYE-DIN
That's a great question and I think that a good example is osteoporosis. Many people would rightly assume that perhaps part of the osteoporosis in coeliac disease is due to the fact that we're not absorbing calcium or nutrients that are important for the formation of bone, but that's only part of the story. The other part of the story is that coeliac disease is an inflammatory immune condition where there's inflammation of the bowel and many organs and we know that with chronic inflammation, longstanding inflammation there's the secretion of cytokines which are the different kinds of chemicals liberated in the body and these can actually have adverse effects on bone and other organs. So for instance interleukin 6 is a type of cytokine that's increased in coeliac disease that can impair bone formation. So it's often a mixture of those things.

SHANE HUNTINGTON
Obviously, problems with bone density are quite severe as we head into our older years. Is it possible for a person to be undiagnosed through coeliac disease, have these bone density problems progressing quite rapidly, but not have the common symptoms that a GP for example might pick up?

JASON TYE-DIN
Absolutely, that is true. We can sometimes diagnose people in older age who have severe osteoporosis and one of the things about osteoporosis is that it's silent until someone breaks a bone. Many people like to think of coeliac disease as a potential ticking time bomb in some ways because you can have this undiagnosed damage going on in the body, whether it's the bones or the bowel causing ongoing issues, but it might not present with symptoms that might trigger investigation for the condition. I think compounding the problem is that when people do have symptoms such as lethargy or bloating or tummy aches they are very non-specific. Lots of people have irritable bowel. Lots of people are tired because of their work/life balance or other reasons, so doctors don't always think of coeliac disease in those situations as well.

SHANE HUNTINGTON
We do a range of standard health checks in many countries. Should coeliac disease, given that context, not be part of those standardised health checks every few years?

JASON TYE-DIN
It's a really good question and I think that the literature is divided on whether standard screening or widespread screening for coeliac disease should take place. The people in favour of that would argue that if you diagnose coeliac disease and treat it then there are clear cut health benefits, but people against that would argue that there's not enough evidence to say that people who have no symptoms who are diagnosed with coeliac disease surely benefit from a gluten free diet. That the understanding of the natural history in that situation isn't well enough understood. So I think that for now selective case finding of high risk people is the way to go, but we need more data to suggest whether population screening is something that we should think about in the future.

SHANE HUNTINGTON
Do we have an idea of how many people are walking around undiagnosed with coeliac disease?

JASON TYE-DIN
Australian studies indicate that about 80 per cent of people with coeliac disease remain undiagnosed and that figure is variable around the world, but in the United States it's thought to be about 90 per cent remain undiagnosed. In Finland where they had a very proactive educational campaign for primary practitioners and screening was much more liberal for coeliac disease, probably about 50 per cent of people have been diagnosed there. So the pickup rate is still very poor and I think it largely relates to the fact that coeliac disease can present with a whole range of different symptoms and coeliac disease hasn't traditionally been on the radar for many doctors.
SHANE HUNTINGTON
You're listening to Up Close. Today we are speaking with clinician researcher, Jason Tye-Din, about coeliac disease. I'm Shane Huntington. Jason, the most important part of the interview of course is what treatments you can offer to patients who present with coeliac disease, what are those treatments currently?

JASON TYE-DIN
So currently in the clinic it's a gluten free diet. So when a patient is diagnosed they come to see me, I will say, okay I will explain what the diagnosis is and then I will send them to a dietician to learn about a strict and lifelong gluten free diet. Now, by removing gluten from the diet as we've talked about, this allows the bowel to heal up symptoms to resolve and the long term complications to be reduced. The gluten free diet is challenging and it does require very strict adherence to be effective and what we are really seeing now is that even after about two years on a strict gluten free diet up to half of adults haven't fully healed up their bowel. So as a treatment it works, but it's not fully effective.

SHANE HUNTINGTON
There are two things here really we are looking at. We are looking at the ability to consume gluten, but also the ability to heal the person who has gone on the gluten free diet. In that second category, are we able to do things beyond just leaving them with time and hoping for the best, or are there studies at the moment that allow us to accelerate or improve that healing process?

JASON TYE-DIN
Yeah, that's an excellent question. I think that the gluten free diet is slow at healing the bowel and traditionally we've just had to grin and bear it, but there is certainly a trial going on now in Victoria in Australia looking at using a medication to try and hasten the healing of the bowel and this is a type of steroid medication which is a topical effect on the bowel with very minimal systemic side effects. This particular agent is sometimes used to treat inflammatory bowel conditions such as Crohn's disease and the hope is with this particular trial perhaps we can heal the bowel very quickly and then allow a person to maintain the healing with a gluten free diet. By healing the bowel we know that the risk of the long term complications can be reduced. So we're basically just achieving our goal a lot quicker and that's the rationale for this trial. It is a placebo and randomised control trial, so we have no idea if it is working yet or not until the study is finished.

SHANE HUNTINGTON
Coming back to the idea of perhaps allowing people with coeliac disease to go back to eating gluten foods, how do we go about achieving that goal? Is there the potential? We're in the century of genomics, to actually modify them genetically or give them something to suppress their immune systems or some vaccine to prevent the onset and get them back to eating as the rest of us do?

JASON TYE-DIN
Obviously, that's the point of our research is to try and find better alternatives to the gluten free diet to allow people back on a normal diet and to have good health. The description of how coeliac disease occurs that I gave earlier allows us to identify several points in the chain of events that we could potentially attack and there are some groups looking at enzymes that degrade gluten. So you will recall that I mentioned that the toxic parts of gluten are often poorly digested. Well, there are some groups around the world in the United States, in the Netherlands and even here in Australia that are looking at enzymes called glutenases that break down those proline residues and break down the toxic parts of the gluten, with the hope that perhaps in the future patients with coeliac disease could perhaps take this enzyme supplement with their meals and it might degrade small amounts of contamination.

Now, this approach would not allow people to have a normal diet. They would still need to be gluten free, but it might allow them more flexibility with a gluten free diet, so that would be great when they are travelling. I think the broader question is treating people with coeliac disease to allow them to have a normal diet and to achieve this it really relies on addressing the underlying immune disorder of coeliac disease and that's where we really need to induce a state of tolerance to gluten. So this is where my research comes in.

SHANE HUNTINGTON
Are you able, I guess one question we could ask is to switch off those genes that are problematic?

JASON TYE-DIN
Yes, the approach here is again borrowing from the allergy world a little bit like desensitisation therapy. So if you can say we know the parts of gluten, the peptides of gluten driving coeliac disease, potentially we could retrain the immune system to switch off that damaging response and become like it was before coeliac disease developed where people can tolerate gluten in their immune system. So our work over the last decade or so has looked at what's driven coeliac disease, those parts of gluten that are toxic and has involved feeding people with coeliac disease gluten ironically, but collecting their blood and profiling that abnormal immune response. We've been able to show that there are just a handful of fragments, gluten peptides within gluten that are responsible for most of the damage that occurs when people eat gluten, wheat, rye, barley or oats. It’s those particular peptides that now compose a peptide therapy which is in clinical trials. Some people colloquially call it the coeliac vaccine and the aim of the coeliac vaccine is to actually induce tolerance to gluten. It's going to be given as a series of injections and hopefully retrain the immune system to become tolerant and allow people back onto a normal diet. So clinical trials are underway and I suppose it's fingers crossed to see where that heads.

SHANE HUNTINGTON
Typically when I speak to a researcher and they indicate clinical trials and so forth, I tell people listening that they should come back in a decade and see how things are going, but you have been working on this for some time. Where are we in that staging of clinical trials, and what kind of timeframe are you able to put on this if it is
JASON TYE-DIN
So the clinical trials are at a level now which is establishing safety and tolerability. The next stage will be to establish efficacy and to determine appropriate dosing. It's a very rigorous process clinical trials and I think that the first step is always to establish that this is a safe approach. Because they are blinded and because they are done in such a way as to keep the investigators blinded to the results, I have no idea how things are progressing except to say that the trials are going ahead and things are moving forward. I guess time will tell.

SHANE HUNTINGTON
So when you're talking about safety, we're talking about human trials though aren't we?

JASON TYE-DIN
That's correct, yes. So these are all human trials. One of the issues with coeliac disease is that there is no real appropriate animal model to study the condition in. The research that we've done here in Melbourne and Australia has been based on human volunteers and it's obviously relevant and appropriate. So we don't have some of the issues related to animal research, but one of the points is that as in many fields of medicine we are moving towards a kind of pharmaco-genomic approach. By understanding a person's genetics we can tailor a treatment to them and this certainly applies to this particular coeliac immune therapy. It's been based on the data we've used for the people with the most common genetic type of coeliac disease which is called HLA-DQ2 and that's in about 90 per cent of people with coeliac disease. We do know that people without DQ2, but have DQ8 respond immunologically to a whole different set of gluten peptides, so they'll need a different version of the coeliac vaccine. So this is targeting the 90 per cent of people with the DQ2 gene, but as for how many people are going to benefit, let's wait and see what the clinical trials tell us.

SHANE HUNTINGTON
Have you ever come across anyone who has presented and positively come out with coeliac disease and then has gone backwards and retracted from that?

JASON TYE-DIN
It's a good question and there's actually some very interesting evidence from a Hungarian study that looked at patients with coeliac disease diagnosed in childhood, who then during adolescence decided to return to gluten in their diet. I think they might have been struggling with the gluten free diet or something like that, and then as adults they were studied and these were adults with known coeliac disease eating a normal diet. The vast majority of those people had not surprisingly damage in their bowel, but 20 per cent of those people didn't. In other words they had so called grown out of disease, but the investigators followed up those people and over time it was shown that many of those people did relapse back into coeliac disease. So at least in the literature there is evidence that perhaps coeliac disease is not always
lifelong, but this predisposition to develop tolerance or intolerance to gluten may be something that flickers backwards and forwards, a bit like a set of scales. Our aim with an immune therapy is to shift the scales towards tolerance to gluten as opposed to intolerance.

SHANE HUNTINGTON
Jason, just coming back to food finally for a moment, why is it that there is gluten in almost everything we find on the supermarket shelf? What is it that requires it to be there?

JASON TYE-DIN
Gluten imparts a great component to food and that's the consistency and it's palatability in many ways. For instance, in bread it imparts that elasticity and doughy nature to bread dough. If anyone has eaten gluten free bread they will know that it's a much heavier, denser type of bread. It often crumbles. It doesn't have that fluffy elastic appearance. That springiness of hotdogs is largely due to gluten. It's also quite sticky so it's often used to stick flavouring onto potato chips. So gluten is almost inescapable from a standard Western diet and we consume about 30 to 40 grams of it every day in a standard diet. As little as 50 milligrams which is 1/100 of a slice of bread can be enough to damage the bowel in someone with coeliac disease.

SHANE HUNTINGTON
If someone suspects that they maybe have an issue with gluten, should they not just immediately go on a gluten free diet? Does that affect our ability to diagnose them later or anything like that?

JASON TYE-DIN
We would not recommend a person starts a gluten free diet without appropriate testing. One of the biggest problems I see in my clinical practice are people who have actually started a gluten free diet. Perhaps they were advised by a well meaning or a friend or a colleague. What that does is that it means that the blood tests used to screen for the condition are not accurate. They're not effective to screen for coeliac disease in that case and the small bowel biopsies we use to confirm the diagnosis again are not accurate. So testing before modifying the diet is very important and many people take the view that perhaps why don't they just try a gluten free diet and see if that helps them from a symptom point of view. What is really emerging from the literature now is that there are many components within wheat and other gluten containing foods that can trigger gastrointestinal symptoms. So a lot of people feel better on a gluten free diet, but that does not mean they have coeliac disease and in fact many people who do feel better on a gluten free diet often have intolerances to other food components such as fermentable carbohydrates within the gluten containing foods.

SHANE HUNTINGTON
Jason, thank you very much for being our guest on Up Close today and speaking with us about coeliac disease.
JASON TYE-DIN
A pleasure, thanks very much for having me.

SHANE HUNTINGTON
Dr Jason Tye-Din is head of coeliac research at the Walter and Eliza Hall Institute here in Melbourne. If you would like more information on this episode, visit the Up Close website where you will also find the full transcript. Up Close is a production of the University of Melbourne, Australia. This episode was recorded on 28 November 2013. Producers were Eric van Bemmel, Kelvin Param and Dr Dyani Lewis. Audio engineering by Gavin Nebauer. Up Close is created by Eric van Bemmel and Kelvin Param. I'm Dr Shane Huntington, until next time, goodbye.

VOICEOVER
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