

The Health Report: 15 August 2005 - Coeliac Disease

[This is the print version of story <http://www.abc.net.au/rn/talks/8.30/helthrpt/stories/s1439372.htm>]

Norman Swan: Coeliac disease used to be thought of as a rare problem where the small intestine of children and adults becomes intolerant to gluten from the diet. The results in children can be failure to grow, and in children and adults malnutrition, diarrhoea, fatigue and even anaemia, loss of periods and rarely bowel malignancy. And as you'll hear there may be a relationship with Type 1 diabetes, the insulin dependent diabetes that starts in childhood and is an auto immune disease.

One of the people who's found that coeliac disease is commoner than many suspected is Alessio Fasano who's Professor of Paediatrics at the University of Maryland School of Medicine in Baltimore.

Alessio Fasano: Yes indeed. We did a gigantic multi-centre study involving more than 13,000 people in 34 states here in the United States. They concluded that prevalence in the general population is more than 1.5 million Americans. And last July the NIH at the Consensus Conference on coeliac disease concluded that if anything we underestimate the disease.

Norman Swan: And apart from failure to thrive in general illness one of the worries with coeliac disease if it's not treated is that you can actually get malignancy.

Alessio Fasano: Absolutely. But even more frightening because of higher frequency is co-morbidity with other auto-immune diseases like damage of the thyroid or Type 1 diabetes or auto-immune hepatitis.

Norman Swan: And what have you discovered that goes on in the surface of the bowel with coeliac disease? What is it about gluten for example that triggers this problem?

Alessio Fasano: Well gluten is a one of a kind protein. We were not built to deal with gluten, that's the reality of the story because you know if you -

Norman Swan: There's nothing in the natural environment, so gluten is an invention of modern cookery?

Alessio Fasano: Well actually it's an invention of agriculture. Nature didn't plan for it. The nature of grains like maize, rice, they don't have gluten in there. When we develop our agriculture 7000 years ago, then we started to mess around with grains and developed wheat then we created a problem. Because of that gluten has a very peculiar effect on the GI tract making the intestine leakier.

Norman Swan: This is in normal people, I mean you and I when we take gluten it has that effect on us as well?



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Alessio Fasano: Everybody. The difference between me and you we don't have coeliac disease and an individual with coeliac disease is that when we are exposed to gluten we have a transient short lived increase of permeability. Very short. While for coeliacs this is a sustained long increase of permeability.

Norman Swan: So when you say permeability you mean the bowel literally becomes more leaky than it should be. And when you say leakier you imagine all sorts of fluids escaping into the abdomen. What sort of leak are you actually talking about?

Alessio Fasano: Well the intestine is covered with a single sheet of cells. Until you know a decade ago so we were under the impression that was completely sealed like cement that would protect us against noxious stuff which comes from the environment. And it's been only in recent years that we understood that actually we don't have a wall there, rather we have a gate that can be regulated and opened and closed if, when and how we like to.

Norman Swan: Which makes much more sense that these cells are kind of rubbing up against each other, have intimate contact but when they fall out with each other they can move apart.

Alessio Fasano: Absolutely. And also this is the way that we sense the environment. In other words, this is the way that we decide when to bring something in so we can assemble it. It's like an athlete who trains for the Olympics, that's what the intestine does. It trains to try to learn about the environment meaning that the immune system of the intestine, it happens to be the largest immune organ that we have in our body, is ready to fight. This will imply that we have to sample what is out there.

Norman Swan: Now what Alessio Fasano and his colleagues have found is that a protein called zonulin seems to control this leakiness of the bowel, this permeability to foreign substances causing, in some people, the immune system to activate against its own body: a misguided missile, which in the case of coeliac disease, misses gluten but hits the intestine.

Zonulin, according to Dr Fasano's theory is an important defence against lots of things we might swallow from the outside world, even viruses. And it may be linked to Type 1 diabetes as well. In other words the bowel is more permeable than it should be to substances (and we're not talking about gluten in this case by the way) which trigger the immune system to attack insulin producing cells in the pancreas.

Could zonulin – indirectly, hold the key to diabetes prevention? Well it depends on which comes first – the diabetes or the leakiness? Dr Fasano and his colleagues did an experiment on diabetes prone rats where they gave them a medication that blocked the effects of zonulin – in other words reduced the leakiness.

Alessio Fasano: So the idea was if we give to this animal in the drinking water this zonulin inhibitor so that we saturate the receptor, in other words put a sort of wax in the hole where the

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key needs to go, are we going to be able to do anything to this animal in terms of preventing diabetes? So we have just regular drinking water, have got this inhibitor in the drinking water and then we followed this animal from weaning – 20 days old. And what we were able to see was that the animal that was prone to develop Type 1 diabetes started to have its own independent leaky gut – it started to leak. At age 50/55 we start to see the other antibodies targeting the pancreas and by age 70/75 they've developed the full bloom of diabetes with the loss of control of glucose. 80% of untreated animals they end up to have this fate. Conversely only 27% of the animals that were treated developed diabetes and these animals did not leak, the permeability was normal, no development of diabetes, no presence of other antibodies. With that, we could conclude with a great level of confidence that at least in this animal model it is the increased permeability allowing environmental material to come in and be misinterpreted by the immune system, leading to an attack to the pancreas.

Norman Swan: Now with coeliac disease you've got to really get off gluten and stay off gluten. If this were to be applicable to the human situation which is a huge if, you're talking about permanent blockade to external sort of things?

Alessio Fasano: Norman I want to stress the concept IF. The issue here is we cannot have the luxury to permanently shut down the system, because nature put it there for something.

Norman Swan: It could be quite dangerous, you might be quite vulnerable to infections or what have you.

Alessio Fasano: Correctly. So what you want to do really is to block the system when there is the danger of something coming through, meaning during the meal and after the meal. Because in between meals it's pretty much there's nothing in there. So the idea is for both coeliac disease and Type 1 diabetes is to develop a system a sort of pill if you like, that people affected by this autoimmune disease, they need to take a few minutes before eating, so that by the time the food is there all the receptor are covered by this inhibitor, the intestinal contents are completely digested so that you know as fragments they would be immunologically not capable to induce an immune response even if they crossed the barrier and that's the end of the story.

Norman Swan: And they've spun out a company to see if such a medication is feasible. Alessio Fasano heads the University of Maryland's Mucosal Biology Research Center in Baltimore.

References:

Proc Natl Acad Sci USA 2005 Feb 22; 102(8): 2916-21. *Epub* 2005 Feb. 14 Related Articles, Links

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I'm Norman Swan, you can hear the Health Report again tonight after the 8 o'clock news and podcasts and MP3 files are available from abc.net.au/rn. And you've got to listen to the program next week, the first in a series of three highly controversial programs on cancer screening. Where finding things early may actually not be the best thing to do, that's a special series from Alex Barrett next week on the Health Report. Now it's time for Life Matters.

Guests on this program:

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