SickKids VS Food Allergy:
The Promise of Oral Immunotherapy

COLD OPEN

HANNAH: Jennifer and her 12-year-old son Ryan have a nightly ritual.

JENNIFER: We put chocolate milk in this little shot glass. And then we open the capsule into the shot glass.

HANNAH: The capsule is filled with peanut powder.

JENNIFER: Then, we mix it around. And then Ryan slurps it. Tell them how much you love it!

RYAN: I love it!

HANNAH: Ryan is being sarcastic. He *hates* the taste of peanut powder. Even the mere whiff of it disgusts him. But Ryan has good reason to hate peanuts. He's *severely* allergic to them. Like, hives-blossoming, throat-closing, get-me-epinephrine-*now* kind of allergic. He has spent most of his life living in fear of peanuts—and working hard to avoid them.

Which begs the question: If Ryan is so allergic to peanuts, why's he eating them every night?

HANNAH: The short answer is that peanuts—the very food that could kill him—might also be the key to protecting him…

OPENING CREDITS

HANNAH: You're listening to SickKids VS, where we take you to the frontlines in the fight for child health. I'm Hannah Bank. And this is SickKids VS Food Allergy.

ACT ONE

HANNAH: When you have a food allergy, the immune system treats the allergen—be it peanut, milk, or soy—as a threat. Like a virus or bacteria that needs to be attacked. For kids with mild allergies, this manifests as everything from redness and hives to coughing and sneezing. For kids with severe allergies, allergens can also trigger anaphylaxis—an extreme reaction that can cause terrible swelling and difficulty breathing. Left untreated, it can be deadly.

There's a good chance that you already know all that. Maybe you have a food allergy. Maybe one of your kids does. Or maybe you're a teacher with a food-allergic student. Because in Canada, we are in the midst of what some call a food allergy epidemic.

HANNAH: More than three million Canadians—and almost half a million kids—have at least one food allergy. That's about one or two kids per classroom. It's hard to know why it's become such a problem, why there are so many kids like Ryan. Because it wasn't always this way. Certainly not in the 50's, 60's, or 70's. And while there is no clear consensus on how we got here, there are some pretty compelling theories. Like this one, which SickKids allergist and researcher, Dr. Julia Upton, explained to me.

DR. JULIA UPTON: When people first started recognizing food allergies in the 1990's, there was this thought that, oh goodness, maybe people's immune systems are too immature to handle foods like peanut. And so the advice was to delay the food.

HANNAH: Turns out, that wasn't such great advice.

DR. JULIA UPTON: One of the most important findings of the last five to ten years is the recognition that the earlier that you eat a food and keep it in the diet, it really appears that you become actually less likely to be allergic.

HANNAH: So, the recommendation to avoid allergens may have inadvertently created an allergy epidemic.

HANNAH: Ryan was diagnosed with a peanut allergy as a toddler. His parents, Jennifer and Steve, aren't too worried at first. Ryan hasn't had a severe reaction yet. So, they're careful, not paranoid. They still keep peanuts in the home. But then, one night, when Ryan is three, everything changes.

JENNIFER: Instant tummy ache. Unable to speak. Trouble swallowing.

HANNAH: She isn't sure what triggered the reaction, but at this point it doesn't matter—Ryan is in anaphylaxis. And time is running out.

As Jennifer dials 911, Steve props Ryan up on the kitchen counter. He's a Toronto firefighter, a man of calm in emergencies. But the prospect of jabbing his own son with a long, spring-loaded needle fills him with fear. Even though its contents—epinephrin, a form of synthesized adrenaline—could reverse the symptoms, and save Ryan's life.

The operator tells Jennifer first responders are on their way. But they don't have time to wait. Steve needs to give Ryan the epinephrine*. Now*.

JENNIFER: And he's like, no, just wait. I'm like, no, give him the EpiPen. Ryan can't say a single word. And, you know, I'm panicking. He's panicking. We're all panicking.

HANNAH: Finally, Steve jabs his son with the needle, flooding Ryan with epinephrine. The symptoms recede. And Ryan begins to come around.

HANNAH: From that point forward, Jennifer manages Ryan's allergy much differently.

JENNIFER: So all peanut products went to the garbage effective immediately. We went from like zero to one hundred in two seconds. We realized how scary and how severe it was.

HANNAH: Reading and rereading labels, quizzing waiters, avoiding playdates—all that becomes routine to Jennifer.

JENNIFER: It's a whole new world; it's a whole shift to teach those around you that love Ryan and love us on how to live and how to be around a kid with a food allergy.

HANNAH: At this point, there isn't any widely available treatment for food allergy. Kids like Ryan are told to steer clear of their allergens—even the may-contain stuff—and carry an epinephrine autoinjector just in case.

So, Ryan does as he's told. He avoids peanuts. He learns to call his mom before eating anything at a friend's house. To separate his Halloween candy into two piles: one safe to eat, and one potentially deadly. It's all very onerous, the anxiety near-constant.

But as he gets older, another approach to food allergy is gaining traction, one that has researchers like Dr. Upton excited. It's called oral immunotherapy. And it just might be **exactly** what Ryan needs.

ACT TWO

HANNAH: Oral immunotherapy, or OIT, is a form of *desensitization therapy* for the immune system. Patients begin by eating tiny amounts of the allergen. Then, over the course of months, and under close medical supervision, the dose is gradually increased.

DR. JULIA UPTON: The overarching idea is that over time you're increasing the amount of food that that your body can see or ingest without having an allergic reaction. It doesn't get rid of the food allergy, but it increases the amount that the person can eat before they have an allergic reaction.

HANNAH: The idea goes back to at least as far as 1908, to an article in the *Lancet* called “A Case of Egg Poisoning.”

DR. JULIA UPTON: Basically someone described way back then that you could alter the reaction that someone had when they ate eggs by doing this oral immunotherapy procedure.

HANNAH: But OIT doesn’t really catch on until the 2000’s, when researchers begin testing it as a viable solution to food allergy. The good news? OIT works. And we’ve seen it firsthand at SickKids. In one trial, patients who once reacted to as little as one or two tablespoons of milk can now chug a glass of the stuff. Which, if you think about it, is pretty remarkable. But OIT is far from the perfect treatment allergists hoped it would be.

DR. JULIA UPTON: When they started doing this, the hope was that if you ate enough of it, you could actually just cure the food allergy and be able to just completely kill those cells, kill that reaction that's going on in the body that recognizes the food as a threat. But that's not exactly what happened.

HANNAH: To stay protected from the allergen, it seems most people need to keep eating the allergen. Although how much—and for how long—remains to be answered.

Then, there's the whole issue of kids with multiple food allergies. It's one thing spending months building up a tolerance to milk. But imagine also doing that for peanuts. And soy. And *fish*. Then imagine having to eat all four of those, each night, as a kid.

But perhaps the **biggest** problem with OIT is the time it demands—of patients, of families, and of allergists like Dr. Upton.

DR. JULIA UPTON: We're called all the time now about people who want to try OIT, people who want to be offered OIT. But it's just so medically intensive that it's difficult to have a wide ability to access this treatment. There's only about two hundred and fifty allergists in Canada. And if each of these people on OIT was to take, a year-ish with a visit every two weeks, I mean, you can imagine the availability gets tied up pretty quickly.

HANNAH: For Dr. Upton, this poses an interesting problem. The treatment works, but it's not a viable solution for the almost 500,000 Canadian kids with food allergy. At least not yet. So, she begins looking at the one variable really slowing things down: *volume*.

DR. JULIA UPTON: There was a really important study where they looked at three hundred milligrams of peanut, which is about a little bit more than one peanut, and they compared that to three thousand milligrams. And they found that the kids were pretty similar in terms of how much could they eat.

HANNAH: In other words, 300mg offered around the same amount of protection as 3,000 mg. But even working up to 300mg can take a year. So Dr. Upton asks herself: What's the lowest possible dose kids need to protect themselves against accidental exposure? Now, finding the smallest dose might not *seem* like a big deal, but think of it like training for a 5K race instead of a marathon.

DR. JULIA UPTON: The lower the dose that you use, the quicker you'll be able to get to that dose, the fewer medical visits that you will have to take to get to that dose.

HANNAH: And the fewer medical visits there are, the more patients allergists can see. This simple, potentially game-changing variation is what makes Dr. Upton's approach so unique. But the tricky part is finding that magic number, one small enough to hasten the treatment, but big enough to protect kids against accidental exposure. Dr. Upton's best guest is 30mg—about a tenth of a peanut. But she needs to test her theory to be sure. So, with the help of her colleagues at SickKids and McGill University in Montreal, she begins to develop a clinical trial comparing kids at 30 mg of peanut to 300mg. The official name is long and academic. But Dr. Upton likes to call it "How Low Can We Go."

Like many clinical trials, it take years of planning. But in 2020, How Low Can WE Go finally begins. And the first patient to enroll is Ryan.

ACT THREE

HANNAH: One of the most important things Dr. Upton has learned from her years as a clinician is that many food-allergic kids don't care about being able to eat peanut butter sandwiches. They just want to be safe. For Ryan, it's as simple being able to eat a doughnut from Tim Hortons with his brother.

JENNIFER: For me it was knowing that he would be safe and not have to live in fear.

HANNAH: But before Ryan can begin OIT, he must complete an oral food challenge at SickKids. First, to confirm he's allergic. (Because, believe it or not, a lot of kids are misdiagnosed with food allergy.) And second, to figure out how much peanut he can eat before reacting, so Dr. Upton can track how much tolerance he builds up over the course of the study. But it's not as simple as eating peanuts under medical supervision.

DR. JULIA UPTON: It's a double-blind, placebo-controlled food challenge, which is a mouthful, but it basically means that he doesn't know and I don't know and his mom didn't know whether he was eating peanut or not.

HANNAH: For a kid like Ryan, who's avoided peanuts all his life, the prospect of suddenly eating it can be daunting, even in a safe space like SickKids. But Ryan says he's game. And so, in a big, toy-filled room on the fifth floor of SickKids, the challenge begins.

RYAN: When I had my first dose, when I got it, I was like, this is not peanut and I had my second, I was like, this is peanut, I had the third. I was like, this is peanut…And then I started to have a reaction.

HANNAH: His gut's killing, his throat's tightening, and hives are sweeping across his back. Plus, he's sneezing—a lot. Dr. Upton injects him with epinephrine to control the reaction. And when that's not enough, she gives him a second dose. Ryan recovers,

but the experience leaves Jennifer badly shaken. At just a third of a peanut, Ryan went into anaphylaxis.

JENNIFER: I just wanted to go home. I was like, so scared for him. And I felt there was mom guilt coming in, parental guilt coming in. Why did we do this to him? Like, was this worth it?

HANNAH: For Ryan, the answer is clear.

RYAN: It was very scary, but I knew that one day I won't have to worry as much about having an allergy, so I was like, I need to keep going.

HANNAH: Soon after, Ryan begins the trial in earnest. He takes his first dose at SickKids—just to make sure everything is copacetic. It is, so Jennifer begins feeding Ryan his nightly dose of peanut powder at home. They experiment by mixing it with Nutella, pudding, and applesauce, before eventually landing on chocolate milk—the least offensive of the bunch.

JENNIFER: I sit next to him for like a half an hour to an hour. Are you OK? Are you OK? Does your tummy hurt? Does your tongue feel weird? You're just kind of like, “Mommy, I'm fine.”

HANNAH: Every two weeks Ryan comes to SickKids, where they check his health and give him his up-dose—a slightly larger amount of peanut powder. Although how much exactly is a mystery to the family. And Dr. Upton. “How Low Can We Go” is what’s called a double-blind study, meaning that Ryan, Jennifer, and Dr. Upton won’t know if Ryan is in the 30mg or the 300mg group until *after* Ryan finishes his second food challenge.

Even though they start small, and work their way up incrementally, the threat of anaphylaxis is always present. Anything from exercise to the common cold can amplify the immune response, triggering a reaction. So when Ryan gets heartburn after a recent updose, Jennifer panics and texts Dr. Upton.

JENNIFER: What is this? What's going on? How do I make this go away? She's like, well, it should get better, but be in touch with me. And like every mom does, you start Googling. So I already diagnosed him with like the worst possible reaction to OIT. And I'm like, could it be this? And she's like, I highly doubt it.

HANNAH: Dr. Upton continues to monitor his progress, and his heartburn resolves. For the most part, that's as stressful as it gets. Until COVID-19 hits. With the new safety restrictions, Ryan can't come to SickKids for his bi-weekly visit. So he gets stuck at his current dose—for four months. But this unforeseen setback may also be a blessing in disguise, a way of bolstering Ryan's tolerance.

Because when Dr. Upton finally hits the unpause button on the study, Ryan sails through his next up-dose—with no heartburn or nasty symptoms. And when I talk to him in December, Ryan has reached the maintenance phase—the highest possible dosage. Which, for him, could be either 30mg or 300mg.

HANNAH: At this point, Jennifer and Ryan already know he's built up some tolerance. Whatever his maintenance dose is, he can eat it without triggering a reaction. But the true test is the final food challenge. Only then will he know which group he's in—and just how much he's protected against the food that nearly killed him.

ACT FOUR

HANNAH: On a grey, bitterly cold February morning, Ryan and Jennifer wait in the hallway at SickKids for his final food challenge to begin.

JENNIFER: Hey, Ry! Are you nervous for today?

RYAN: Kind of.

HANNAH: Ryan has good reason to be nervous. During the last food challenge, his reaction was so bad he had to be dosed with epinephrine. Twice.

HANNAH: Ryan is called into another room, where Dr. Upton is waiting. He plops into a big blue chair. A yellow clothespin is clamped on his nose. Then he's handed a tongue depressor with a big wad of what looks like mud flecked with rice. It's another double-blind, placebo-controlled food challenge. So he's not sure if it's peanuts or sunflower butter. But he is sure it's gross.

Ryan gags.

DR. JULIA UPTON: Can you do it?

JENNIFER: Close your eyes, close your eyes.

RYAN: Look what's in there!

HANNAH: Ryan takes it down in a single gulp. And for a second, it looks like he might puke. But he doesn't. Nor does he react.

RYAN: That was not peanut.

JENNIFER: Well it might not be.

HANNAH: Turns out it ***was*** peanut. Which becomes clear when Ryan starts to break out in hives. **But that's *it***. No gut pain, no throat tightening.

JENNIFER: No anaphylaxis, which is insane for us… They gave him some sort of antihistamine for kids, and he chilled out for a while and then it passed.

HANNAH: Ryan was able to eat **more than seven peanuts** with only a mild reaction. Which means he's well protected against accidental exposure. For Jennifer, it's the best possible outcome.

JENNIFER: It just changes things like my anxiety level and my fear level of for him you know.

HANNAH: Dr. Upton now knows if Ryan was in the 30mg or the 300mg group. But she can't tell me, not without compromising the study. Still, she **can** tell me that she's thrilled for Ryan, who no longer has to live in fear of peanuts. Thrilled for Jennifer, who no longer has to worry about anaphylaxis. And thrilled at the promise of low-dose oral immunotherapy, which could help keep countless kids safe from food.

EXTRO

HANNAH: From SickKids Foundation, this is SickKids VS. Thanks for listening. If you want to support work like this, visit sickkidsfoundation.com/podcast to donate. And if you like this podcast, please subscribe and rate us on Apple podcasts, Spotify, or wherever you listen to SickKids VS.

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Oh, and please don’t try oral immunotherapy at home. Not without the supervision of a seasoned allergist like Dr. Julia Upton.