Benyamin Cohen:
Hello, and welcome to another episode of the "Hadassah on Call" podcast. I'm your host, Benyamin Cohen. If you have allergies, and most of us do, you're going to want to listen to today's episode with Dr. Yuval Tal, the director of the Allergy and Clinical Immunology unit at Hadassah Hospital. We're going to be talking about those common allergies we're all familiar with, dust and pets, for example, but also some you may have never heard of. We'll talk with Dr. Tal about how his team invented a way to help a child suffering from an allergy to light. Plus, Dr. Tal gives us a sneak peek of the allergy medicine of the future. Hello, Dr. Tal. Welcome to the show.

Dr. Yuval Tal:
Hello. Very nice to be here today.

Benyamin Cohen:
Thank you so much for joining us. You're at, you're at Hadassah Hospital in Jerusalem right now.

Dr. Yuval Tal:
Yes. I'm in Ein Kerem, Hadassah Hospital right now, in my office.

Benyamin Cohen:
Well thank you for taking the time to chat with us today. We really appreciate that. So you are an allergy expert and we want to talk to you about all sorts of different allergies, but just to get started. What are some of the most common allergies? I know growing up, I heard about dust, or pollen, or ...

Dr. Yuval Tal:
Allergy is like one arm of the immune system, autoimmunity diseases that the immune system attack the host, or immune deficiencies, or acquired, or native immune deficiencies on other parts. But allergy
is the major, major area that we deal with. And we have a amazing experience because we are huge center now.

**Benyamin Cohen:**
So, tell me what are some of the most common allergies that you see?

**Dr. Yuval Tal:**
So the most common allergies, of course, allergic rhinitis and asthma, which take us back to the pollens, or animal allergens, like cats, dogs, or house dust mite, if you are thinking about house dust mite, you are not allergic to the entire insect, but you're allergic to two small protein in the stool of the mite. It's not fun to be allergic to her stool, but this is the fact. And this is a very, very common worldwide allergy. We have here olives, that make significant allergy more than other allergies that are more common in the States, for example.

**Benyamin Cohen:**
You said olives?

**Dr. Yuval Tal:**
Olives, olives, flowers, small yellow flowers of the olive trees.

**Benyamin Cohen:**
Oh wow. Wow.

**Dr. Yuval Tal:**
Which is very, very common allergy here. And we have trillions of olive trees. It's very common allergy. Grasses like in the U.S., but different grasses. But inhaled allergen are not the only allergy of course, we have plenty of drug allergies, like all around the world. We have food allergies, we have bee stings, hymenoptera allergies. We have weird allergies like in the rest of the world. And we might talk about them eventually later.

**Benyamin Cohen:**
How do you know ... I mean, I have this issue sometimes when I wake up in the morning and I feel a little congested and I can't tell if it's just an allergy or if it's a cold. Is there a way to know the difference?

**Dr. Yuval Tal:**
Yeah, the first clue is that viruses die. So, it's gone in a few and if it's repeated at the same time of the year for month, it is probably not a cold. Common cold, which mainly caused by viruses like rhinoviruses, in short, this is you have fatigue, you have muscle ache, you have more than just running nose in many cases, and it will not respond to antihistamine in many cases, especially not to new generation antihistamine. We don't give drugs similar to Benadryl in Israel anymore, or around the world. But in the U.S., it's still very common. We use more next generation, which doesn't make you fatigue. So, the fatigue and the muscle ache and the weakness is a part of viral. And it's short-lasting, it'll take three to five days to go.
Allergy is an inhaled allergy because of flowers, as long as you have the flower there’s an allergen in the air, so it will not go away. And then you have special signs and symptoms, you have a running nose or stuffed nose, must probably stuffed nose. You have runny nose, itchy ears, you have itchy nose that you want to stick a pen inside and it doesn’t get there, you know?

**Benyamin Cohen:**
Yeah.

**Dr. Yuval Tal:**
Itchiness in the throat, you see that patient trying to scratch inside and can’t do it. So, you have what you see as a specific phenotype. Usually, you can tell it’s allergy and your household, your family has ... most probably some of them has it as well, because it’s very, very, very genetic disorder. If your father has, half of the children will have it, probably.

**Benyamin Cohen:**
That’s my next question, yeah. Are allergies something you’re born with or is it something you develop later in life?

**Dr. Yuval Tal:**
You’re born with the tendency to develop allergies. Which mean you have a special IgE, which is the antibody that activates some part of the system. But if you are being exposed again and again, to the same allergen that you have tendency to develop antibodies against, you will have in many cases, disease, in many cases, only markers. But for instance, you can’t get allergic reaction, which mean what you said about allergen, airborne allergens, it’s immediate type allergy. So, that mean you need it to happen once, but you need repeated exposures. Which means if it’s a first time that you see a dinosaur, so you will not have an allergic reaction, only if you have encountered repeated exposure, which vast enough different gaps between the time you met the allergen. So, you need repeated exposures and inherent tendency to have it.

**Benyamin Cohen:**
So, if I’m allergic to cats and if I see a cat once, you’re saying, I probably would not have a allergic reaction?

**Dr. Yuval Tal:**
The first encounter will do activation of your tendency. Only second will make mast cell to degranulate and release the histamine, which make you most of the phenotype.

**Benyamin Cohen:**
Interesting. Now, is there speaking of cat allergies, is there a difference biologically or chemically between allergies like dust and nature allergies versus like a pet allergy?

**Dr. Yuval Tal:**
Actually, there are some minor differences. A cat allergy, as opposed to flowers and it’s harder to treat because it’s a strong allergen. Actually, the room that the cat lived in could be allergenic for six months after he died. There are some kind of proteases, substance that degrade protein and stuff in the skin of
the cat, which flower doesn't have. So, we usually don't mix animal allergens and flower allergen for the 
immune allergy shots, you know?

**Benyamin Cohen:**
Yeah.

**Dr. Yuval Tal:**
We don't mix them because of the proteases and stuff that the animals has in addition. But generally mite are animals, and it's very common and it's not so far away in phenotype from allergic due to pollens, but pollens are seasonal in most cases and cats not.

**Benyamin Cohen:**
Right, we're talking about some of these common allergies, but I know there's so much of what you and your team do at Hadassah, so I want to try to cover a few different areas of allergies. I know one of the things actually that caught my attention, obviously we're still in the pandemic and we're still dealing with COVID-19. I think you did some research along with Harvard Medical School about the racial differences in COVID-19 mortality rates. Can you talk about that?

**Dr. Yuval Tal:**
It's very comfortable, Harvard School, it's my sister. So actually, she was a doing angiogenesis, which mean blood vessel. And then we switched to clinical immunology and allergy because she had fascinating results regarding Black and white American. We knew that there are plenty of different diseases or situation that Black Americans are more affected, more easily, or more severely affected with it. So, people were saying it's because they have a situation and their population, which meant the condition of life. But it was too much. If you look at the COVID, and you'll see what the authorities in America said, you see that in some cases, there are four to five times Black American death from COVID compared to the white population. And then you reduce the tendency to diabetes, and blood pressure, and closeness to health facilities.

**Benyamin Cohen:**
Hospitals, yeah.

**Dr. Yuval Tal:**
Yes. Then you could reduce it by half and still you have two and a half times. So, my sister called me and said, "I have a lot of protein-"

**Benyamin Cohen:**
Wait, just to clarify your sister's at Harvard?

**Dr. Yuval Tal:**
Yes, yes. She called me, "Now, after you convinced me to switch to clinical immunology and allergy, I have a lot of protein that raised up in the difference between Black and white. I need to know what to concentrate on." I was thinking about which maladies, natural disease, are more common in Black Americans? And we started thinking about atopic dermatitis and asthma and allergic rhinitis were much more prevalent, more severe. We have lupus, systemic lupus erythematosus, which is an autoimmunity,
which is more prevalent in Black American and more severe. Black American dies more from sepsis. They have more tendency to catch COVID.

So, we utilize the COVID to publish the first paper, because I told her, "I know what disease Black American has more. Now, let's look at the drug that inhibit them." Biological drug that inhibits specific protein. And if you are doing an anti-allergic drug, like dupilumab, you inhibit protein called four and 13 doesn't really matter. But I told her, "Look at protein four and 13 in your list and if they are higher, look at the statistical significance."

So, we pulled out everything and we managed to show, my sister managed to show, that low pigmented melanocytes secreted a method that called fibromodulin and if fibromodulin is high, it expressed more TGF beta, which is an inhibitor protein and then cell S, a very, very important cell that caused dendritic cells in the skin getting activated in Black Americans, because there have less TGF beta.

So, that's how we found a large family of protein that are highly expressed in Black Americans when you activate dendritic cells, and dendritic cells been activated much more easily in Black Americans. That's why they have more atopic dermatitis, and allergic, and asthma and whatever you see more prevalent in Black Americans, and we found a molecular basis for it. So, you could be a personalized medicine for Black Americans, lupus, which will more be more appropriate than for white American and vice versa. This was the first step. Now, we're doing each disease separately and proving the same mechanism with dark and white mice and then human tissues. But it's really, really, really is there, and we have a huge success in this area.

**Benyamin Cohen:**
You're saying you could treat each person differently based on their own needs?

**Dr. Yuval Tal:**
Personalized medicine is the future, which mean if you have high ... I'll give you an example, totally different one. Sometimes in oncologic patient, there is treatment resisting pruritus. They have pruritus all day every day, day, night until I met some oncologic patient which were at remission. And they said, "I prefer to die from the cancer, so it stop scratching." I got a phone call from a professor here, and she told me, "You must help me. The patient would prefer die instead of keep getting pruritus and scratch every day at night, they prefer die from the cancer and finish it all. You must help me. He doesn't respond to steroid. He doesn't respond to antihistamine. He doesn't respond to phototherapy."

So, I told her, "What do you want from me? It's not my area. I don't know." She said, "I know you can help me. You'll help me." So, I really got frightened because she's very frightening. So, I tell her, "You know what, write she has atopic dermatitis. You are a dermatologist and an oncologist. She has atopic dermatitis, which is a skin disease, allergic atopic skin disease. And I'll try to do the rest." So, she came to me, and I gave her a certain drug that called dupilumab, which inhibits proteins four and 13, that we previously discussed about. If you have high four and 13 protein, interleukins four and interleukin 13, you eventually will have high interleukin 31. Interleukin 31 is the itch protein, itch cytokine, itch cytokine. So, if you'll inhibit this, you can break the vicious cycle of pruritus which will not respond to steroid, we will not respond to antihistamine or phototherapy. So, we get her dupilumab like she has
atopic dermatitis because it’s indicated for atopic dermatitis and we inhibit interleukin 31 and three treatments later, a month and a half later, I saw her again. And the pruritus gone.

Benyamin Cohen:
She was no longer itching?

Dr. Yuval Tal:
Yes, and then we initiated a large cohort of a treatment resistant oncologic pruritus which make the hell for the patients and we are giving them dupilumab.

Benyamin Cohen:
Wow.

Dr. Yuval Tal:
And eventually we have a huge success in preventing the life agonizing pruritus of those very, very poor patients. And what I said before, it's personalized medicine, you know?

Benyamin Cohen:
Yeah.

Dr. Yuval Tal:
I’m treating the overproductive protein in this specific patient, like we now starting to have in asthma. We can kill the eosinophils separately by specific drug, or we kill the IgE that make allergy. And we can kill the protein four and 13, which will make the allergic response. Eventually we can kill other protein like [inaudible 00:15:34] which is on pipeline, and we can deal with each asthma according to its phenotype. We don't do it very well. Yes, we're guessing. But eventually we'll have markers that we can choose the right medication for our asthma patient. Allergic rhinitis is somewhat easier, but nasal polyposis, it's another devastating life quality for the patients. And we can actually kill it.

Benyamin Cohen:
Wow.

Dr. Yuval Tal:
With this specific medication, biological medication. We are doing it with a lot of medication. You heard the question earlier when we discussed before the podcast, about certain cases, and I have an example for personalized medicine. We had a 45-year-old male from the north that came to us after he was in the hospital in the north with a situation called eosinophilic cystitis, which meant that his urinary bladder was like an apple full of cells called eosinophils and he couldn't urinate. So, he had two nephro stones, two tube in the renal, in the kidneys to evacuate the urine, and he couldn't pass urine. Yes?

Benyamin Cohen:
And what was the disease he had?

Dr. Yuval Tal:
It's called eosinophilic cystitis. It's very, very rare, which the gall bladder is full with cells that called eosinophils which is allergic arm of the immune system cells. They found five parasites and stuff like this, so it shouldn't be there. And they went to a nurse, and they said, "We have a great solution for you, which is radical testectomy," which meant that they will cut out the urinary bladder and make a like urinary bladder from the intestine itself. So, the patient will do self-catheterization until they'll have sepsis and die, or whatever. And he was only 45, previously healthy and he came to Hadassah for a second opinion.

So, I told you, "You know what to do. We have a certain biological medicine that kills eosinophil on spot." On the same day, we gave him the medicine after we signed some forms and stuff like this, because nobody gave it ever, but we have it in the fridge for asthma patients. We get the proper papers, and we gave him the first injection. And after three weeks, he was calling my fellows crying. He started passing urine.

Benyamin Cohen:
Wow.

Dr. Yuval Tal:
Last January, a year and half ago, he came back to urologic department. They did an exam, there was a normally functioning and histologically, normal urine bladder. And he was healthy, with his own urine.

Benyamin Cohen:
Yeah, that's unbelievable.

Dr. Yuval Tal:
It was the first case to be reported. And since then, we have more new indication for the same drug, for incurable, previously incurable disease. We just open new labeling for this medication, but actually we need to save our patients. Because if you close your eyes and try to imagine the immunological process, you can stack it in the way, with the new generation drugs and this is our strongest ability we know to stop rare diseases from actually manifesting.

Benyamin Cohen:
When we return, Dr. Tal talks about fascinating research his team is working on to help women who are allergic to semen. Turns out it was the men who needed to take medicine. All that, and much more after the break. If you're enjoying this episode, you'll want to check out our previous conversation with Dr. Gurion Rivkin, who heads the joint replacement unit at Hadassah Hospital. We talked a lot about knee and hip replacements and how a new robot called the ROSA is helping them perform better surgeries.

Dr. Gurion Rivkin:
The reason the industry, the medical industry, developed robots now and computerized assisted surgery before, was because with knee replacements, we had a problem. Our satisfaction rate is only 85%. And so, you can say that's a big number, but that leaves 15% of unhappy patients. And when you have that kind of percentage on a surgery that is performed on millions of patients around the world, that's a big problem. And that's why we're always looking for ways to improve our results.
Benyamin Cohen:
You can find that episode of "Hadassah on Call" on Apple Podcast, Google Play, or wherever you get your podcasts, or on the web at hadassah.org/hadassahoncall. That's hadassah.org/hadassahoncall. And now, back to our conversation with allergy expert, Dr. Yuval Tal.

It's interesting. We started this conversation talking about common allergies, dust and pets and things like that, but oftentimes, people don't realize that the allergies manifest themselves in so many other places. I was reading, when I was doing a little research for this conversation, I learned that women can sometimes be allergic to semen and that your department at Hadassah has come up with some ideas to help with that. Can you explain that a little bit?

Dr. Yuval Tal:
Well, it is old, not so old, but a few years back, but we just recently reopened it because apparently the gynecologist doesn't know it. So, we presented to them, and they said, "We have thousands of women like this."

Benyamin Cohen:
Wow.

Dr. Yuval Tal:
But it's not allergic. It's not an allergy. Semen allergy, which is an allergy to a certain part of the protein in the prostatic specific antigen, the PSA that you measure for prostate cancer and stuff like this, it's very rare. It's like one in a million. We have like a hundred cases in the literature since forever and probably most of them are not really allergic but misdiagnosed. But I had a young couple came to me a few years back, with the female had ... they were religious Jews, so it was the first partner. So, they didn't knew if it happened before. She had a pain after ejaculation, post-ejaculation pain, repeatedly from her spouse. We asked her to do it with a condom to see if it's the friction itself or the semen. So, it was gone with the condom, but when they removed the condom, it reappeared. So, we asked them to take antihistamine medication, maybe it's allergic to ... Everybody in the world said it's allergic, for the last 60 years it has been described allergic disease, but then I thought it couldn't be allergic. It's like everybody does it.

I had a clue. I had a clue because I knew there is a certain protein in the semen that's called prostaglandins. Like you take aspirin to inhibit inflammation because you're stopping prostaglandin production, you understand? Prostaglandin make inflammation, but they're in the seminal fluid because that it enable the sperms to move better. So, I said, "Just a minute, prostaglandin are allergic mediator," which mean they cause vasodilatation, increase the diameter of blood vessels in order to ... inflammatory cells to get out of the blood vessels. So, if I inhibit prostaglandins, so I reduce the inflammatory protein in the semen. So I said, "Okay, I can prove that it is not allergic, but a reaction to prostaglandins that normally resides within the semen."

So, we chose two healthy volunteers. I will not go into detail because it's embarrassing and we took the seminal plasma and diluted to men which cannot be allergic to their own seminal plasma, or almost never, but let's say never. I'll skip the many, many details in a way. And we injected them intradermal their seminal plasma without the cells, and they had a huge, huge skin response, which was not itching,
but was actually painful, like when you have a smaller fingernail, and you take it out and you feel your pulse in here and it's very painful.

So, it felt like inflammation and not allergic response. So I said, "I can prove it." I asked the volunteers, so-called volunteer never mind, to take aspirin, which inhibits prostaglandin production, also in the seminal fluid and after a week or so, we repeated the experiment. They gave us fresh seminal plasma and we injected it to the skin and the skin test then disappeared. So, I said, most of women which have pain after coitus, local pain, suffering from probably a reaction to the prostaglandin, an autologic reaction. So, I gave the male aspirin, not the female, and after a month or so, they stopped having the pain after coitus because they were-

Benyamin Cohen:
The woman stopped?

Dr. Yuval Tal:
The woman stopped because she-

Benyamin Cohen:
Wow.

Dr. Yuval Tal:
... because he had less prostaglandin in the seminal plasma.

Benyamin Cohen:
Wow. That's just fascinating to think that you're giving the medicine, not to the person who's suffering, but to the other person.

Dr. Yuval Tal:
No, actually, actually for the last 60 years, everybody called it allergy, and everybody was testing the female, for the skin test on their female, but nobody thought about ... I'm a biologist, so I thought about where's the control? There is no control in this test. So, I choose the husband as control, and he was as positive as the woman. So, it was truly not an allergic response.

Benyamin Cohen:
Wow.

Dr. Yuval Tal:
So, I knew that for the last six years, the world had a mistake about seminal plasma allergy and I wrote it with Jonathan Bernstein, which is a very, very famous Jewish professor of allergy in Cincinnati. And we published it in a very, very big clinical and allergy journal, a few years back and now we're doing the big experiments in real women across Israel.

Benyamin Cohen:
Not necessarily related to this specific allergy, but in general, do you see ... are men or women more likely to have in general, just allergy reactions?

**Dr. Yuval Tal:**

In some areas, female are more prone to have it. If you look at the COVID Pfizer immunization vaccine, you can see that female state they had an allergic reaction, more common than men, but it's very, very common about many medications, that female complains more about allergic reaction than men. But if you think about it, you understand that the female and male get the same dosage of medication, but female usually are much smaller. So, perhaps something is a bias of our pharmaceutical company, or ourselves as a physician, and not necessarily from the gender differences.

However, in asthma, the prevalence change from higher in children, girls to boys ratio, and then they switch in adulthood. And we can see some kind of kinetics, but since female has more flexible immune system, which enables them to carry a child and maybe they have more ... So, they have more tendency to autoimmunity because if they can tolerate the child, they need to be less harsh about themselves as well. So, they form auto antibodies, which responds against themselves and make autoimmunity, which is much, much, much more prevalence in female, and for the first section of our talk, Black female, even more.

**Benyamin Cohen:**

Are stress and allergies linked?

**Dr. Yuval Tal:**

Okay. The literature, we said, we have no ... We know close that it's linked, but it's not true. I think it's not true. Many, many cases in a jurisdiction, in a judge, jury, whatever you call it, in court, try to claim that we have serious stress from the army, or serious stress from a car accident, and then we develop allergies and we're suffering from it severely. And it never, never was a successful claim in court. However, in the last few years we see a huge connection between so-called mind and body. I don't know if it's mind, or if it's hormonal, or if it's God, I don't care, but I can tell you my story and the only side.

I can tell you before I'm telling my story, that it was well published in one of the biggest immunology paper in the world, so it was accepted. It's a long story, so bear with me. It all started with a child, five and a half years old. The child has a weird case of allergic rash, which could not be explained by nothing, because there was no trigger, but any time that they get out of the house, he was getting a rash and feeling fatigue and feeling very bad. Eventually it was diagnosed as solar urticaria, which means allergic reaction to light.

**Benyamin Cohen:**

Wow.

**Dr. Yuval Tal:**

It's a certain wavelength of light, in each patient it could be different, but it's in the case, it was visible light, which make him a harder case. Eventually, he made an anaphylactic shock in beit knesset, in the
synagogue in the Simhat Torah, which is a holy Jewish ... and he had anaphylactic shock due to fluorescent, indoor fluorescent light.

Benyamin Cohen:
Wow.

Dr. Yuval Tal:
Indoor florescent light. So, they brought it to here, to the hospital and the dermatologist brought the children to us and asked us what to do. Eventually we decided to give him anti-asthma medication, which was approved only for asthma and only for adults, because we heard about an adult case in Germany and we had no other solution, nothing worked. And the child have life-threatening disease, which is very, very, very, very rare in solar urticaria. Usually, they have only rash. So, we gave him one quarter of a bottle, very frighteningly. I tied into my leg and worked with him for the entire day in the hospital and then it did nothing.

Two weeks later, we gave him an whole ampule, a one and a half ampule and then twos ampules, which is a dosage for an adult. Anyway, about two months later, we kept giving him every two weeks, 300 milligrams, which we got from an army guy that stopped taking it, nevermind, crossed out after that [inaudible 00:31:51]. And his mother sent me a picture of him in the desert, on a camel in the middle of the day. I still have shivers now when I'm thinking about it, his picture on a camel in the desert, in the middle of the day. He's very, very pale boy. So he had a hat and long sleeves, but nevertheless, it was amazing. So, he was keeping getting it. His mother is a professor of psychology, she is an expert on PTSD, post-trauma stress disorders.

So, I went to asked her, maybe the child has some kind of anxiety disease. He's getting out of the sun and make anaphylactic shock. And maybe there is an anxious strategy or something? So she came and tell me, "The boy is fine, but I couldn't find anything about post-anaphylaxis PTSD." I told her, "This is nonsense. Everybody has PTSD. You have PTSD from bullying at school, from holiday season, from getting divorced. He must have, I can prove it."

So, we took our hymenoptera allergy, which is bee sting allergy patients who's getting immunotherapy for bee sting allergy and a patient that came to the ER with a large local reaction after bee sting and were frightened enough to go to the hospital and check them. And we saw that 70% of the men that had anaphylaxis after bee sting had a probable PTSD, which was not diagnosed. So, we proved it everybody ... but you need previous psychological insults. A car accident, harassment, or stuff like this. And after, you had a few, it's the sting that is a straw that broke the camel's back.

Benyamin Cohen:
Yeah. In America, we don't have camels, but yeah.

Dr. Yuval Tal:
Yeah, but you understand what I meant?

Benyamin Cohen:
I know, I know. I'm kidding.

**Dr. Yuval Tal:**

My student came to me and said, "If you switch it it's like when you are having more stressful event, you eventually will have more prevalence to do anaphylactic shock." I said, "It is nonsense. It is statistical nonsense." Then I came back to him and said, "Wait, don't write it's nonsense. I'm not sure I'm right. When we have an action patients, it is harder to balance their asthma. It is harder to balance the urticaria rash, their hives, or their atopic dermatitis. Wait a second, let me check the literature." I went back to the literature and indeed, more stressful patients are far harder to balance their allergic diseases.

So, I went back to the literature after talking about it in a convention and found a mice, rats that were sensitized to egg protein, allergic sensitized to egg protein. And then they put in a cage, and they had an aerosol, which is a shower of water and egg allergen, together with high noises and lights, like frightening surrounding. And they had anaphylactic shock and then repeated, repeated again and then another time they had anaphylactic shock and the first time, they took half the group and put them in a aerosol of water, or saline, never mind, water, salted water, and a aerosol of an egg. And then both cages had hard noise and sounds, and lights and both groups had anaphylactic shock, without allergen itself. And the researchers said it was Pavlovian reaction, which is like psychological reaction. But then they described the pets, the rats, and they were sneezing. They were gasping for air. They were scratching themselves. They had truly anaphylactic allergic, histamine mediated, allergic reaction. It was not like they were confabulating it, they are rats. It was the wrong conclusion.

I went out to the hospital and met a fellow, a professor of psychology of mine. Said, "I had a very weird result in a PTSD and anaphylaxis." So, he said, "Wow, it's amazing. We just published an article about young adults that had been participant in terror attacks during childhood. Half of them with PTSD and half of them without PTSD. And we checked for various immune-related proteins in the blood, and there was some kind of nonspecific increase in some protein in the blood. Would you like me to send you the article?" He said. I said, "Yeah, sure. Send me the article." I looked at the protein that were elevated in the blood, and it was not like nonspecific elevation. One protein were much, much higher than the rest, which was IL-4, you know IL-4, the four protein that we mentioned before?

**Benyamin Cohen:**

Mm-hmm.

**Dr. Yuval Tal:**

It's the main protein of allergic reaction. So, if chronic stress increase the IL-4 level in the blood, allergic diseases will become more treatment resistant. So, we have a mechanism, and we publish it. I thought they will throw tomatoes at me on the stage, but they really, really liked it. So yes, I think it's related. I think there is much that we don't know about psychological state and immune-mediated diseases.

**Benyamin Cohen:**

So, did this, going back to the story, did this five-year-old kid have some kind of stress PTSD from something?
Dr. Yuval Tal:
No, he was fine for about 10 years. And then he gradually stopped responding to the original medication. So, four weeks ago, we were able to obtain the next generation of the old medication, which is not prescribed anywhere in the West, but not approved in the FDA even. And the company was generous to give us a box of this medication to give the child. And we gave him just the first medication because it took like six months to approve it by ministry of health and stuff and cross your finger it will help.

Benyamin Cohen:
Wow.

Dr. Yuval Tal:
I think it could do the job again.

Benyamin Cohen:
Wow.

Dr. Yuval Tal:
And give him life again.

Benyamin Cohen:
When we return, Dr. Tal talks about his hopes for the future of allergy research. All that, and much more, after a quick break.

As one of our podcast listeners, you've been hearing all about how Hadassah is here, healing the world. Every day innovations from Hadassah's Hospitals save lives in Israel, the U.S., and around the world. Being a member of Hadassah means you're a part of it and that's something to be proud of. Hadassah is here for you, here for each other, and here for the world. Learn more about the many advantages of membership at hadassah.org/hadassahishere. Membership starts as low as $36 a year. If you're already a member, think about making someone you love a part of our healing work. Membership makes a beautiful gift. That's hadassah.org/hadassahishere. And now, back to our conversation with allergy expert, Dr. Yuval Tal. So, is there such a thing as a cure for an allergy?

Dr. Yuval Tal:
We are getting better. We have three level of treatments. The first is blocking the substance itself. We can give nasal spray, antihistamine and block it for seasonal allergic rhinitis and improve the quality of life. Second, we can block the immune system, which mean if you have seasonal allergic rhinitis and I will give you omalizumab, anti-IgE at the beginning of the allergic season, I could block the entire effect for most of the season, if not all. There was just recently a huge Chinese article about it, which proved that it's the same, even for the forest. So, for other races, not only for us, and we gave it to a few patients that really desperately needed it, and it worked. We can block the entire arm of the immune system for three months or for two months and then there's no more flower, no more allergen and everything is cool.
But the best solution is still immunotherapy which currently is by injection. And for house dust mites for example, it's almost 70% cure, which will mean if you don't have allergic rhinitis, you will not have allergic asthma exacerbations or less and it's very, very important for life quality and for life itself, not just quality, because asthmatic could be life-threatening situation. Now, we have for many allergen, sublingual immunotherapy. So, instead of the injection, you put a small tablet underneath your tongue and it dissolves very rapidly and you have the same effect of immunotherapy. Immunotherapy is not like getting your body used to it, it's like getting it to learn that it's not dangerous and it will stop response. I will not go get into the mechanism, but it has a memory. Memory T-cells and it'll stop responding for a lot of years if not forever.

So, a very large percentage of the population’s response, cats, if we ... I mentioned it earlier are the hardest to treat. They are very vicious allergens. So, it's better to give the cat somebody else or something, because it's very, very hard to get rid of cat allergy. But for house dust mite, which is far more prevalent, it is feasible.

Benyamin Cohen:
I mean, you keep saying that there's new stuff. You were just talking about giving this new drug to this kid. If you and I were to have this conversation in five years, in 10 years from now, where do you hope to see the treatment of allergies?

Dr. Yuval Tal:
Oh, we started talking about it earlier and actually, it is going to be personalized medicine. We can lower the flames from an overactive immune system arm if it's autoimmunity, if it's allergy, we can even try and help certain immune deficiencies in the same way.

Benyamin Cohen:
We just have another minute or two left. It sounds like so much of what you're doing is research oriented and you've been able to really help patients that no one else could help. Is that what makes Hadassah unique?

Dr. Yuval Tal:
Actually, actually, my friends, my beloved friends in the unit, are amazing, amazing doctors. We are now in Hadassah, 11 clinical immunologists. Which mean in Israel, in the entire Israel, there are 100 and we are 11 only here and they are doing magic, they are so, so clever. They're so amazing human being and doctors, and they give their soul to the patient. Humility and caring is the key to overcome the diseases. Ask anybody, search anybody, don't ever give up on your patient. And they find the most amazing solution for the patients. Like I told you, you're closing your eyes, you imagine the immune system and you see there is the solution, and this is our strongest point.

Benyamin Cohen:
Yeah. It's thinking outside the common ... you're thinking outside the box a little bit.

Dr. Yuval Tal:
Yes, yes.
Benyamin Cohen:
I always like to end my conversations by asking, is there anything I did not ask you that I should have asked you?

Dr. Yuval Tal:
Actually, actually I thought about it and the answer is yes, like a million questions, but we don't have the time now because it's an amazing profession. It's a huge profession and it's amazing profession. It's getting bigger each day. So yes, probably there are a million of questions you didn't ask. But we gave a taste from our work and our doing here and it was fun.

Benyamin Cohen:
Well, thank you. I really appreciate you. I know you're a very busy doctor and heading up the unit there. So, I really appreciate you taking the time to talk with me and our listeners today.

Dr. Yuval Tal:
Thank you. Thank you very much. This was great being here today.

Benyamin Cohen:
"Hadassah On Call: New Frontiers in Medicine" is a production of Hadassah, the Women's Zionist Organization of America. Hadassah enhances the health of people around the world through medical education, care, and research innovations at the Hadassah Medical Organization. For more information on the latest advances in medicine, please head on over to hadassah.org/news.

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The show is produced by the team at the Hadassah offices in both New York and Israel. I'm your host Benyamin Cohen and thanks again for joining us today. We'll see you next month.