Ask A Biologist Vol 080 (Guest Paul Turke)

Rebooting the Immune System

Remember your last paper cut, or the bad cold that had you coughing and blowing your nose? It was your immune system that was busy battling the bacteria or virus that was attacking your body so you could get well. How your immune system works is the discussion Dr. Biology has with pediatrician **Paul Turke**. They also talk about how our immune system has to reboot to keep up with evolving bacteria and viruses.

Transcript

Dr. Biology: This is "Ask A Biologist," a program about the living world, and I'm Dr. Biology. Let's talk a bit about something very important to all of us, "Our immune system."

Now in case you missed it in class, our immune system is our defense against attacks from things like bad bacteria and viruses. It helps us keep from getting infections when we get a cut. It also helps us battle things like the common cold, and it defends our body from much nastier diseases.

In Ask a Biologist, we even think the immune system is so important that we created a comic book on the subject. It's become a favorite of kids of all ages. It's called "Viral Attack," and it tells the story of how a collection of special cells protects you.

It includes, among others, the macrophage. Macrophage, it's kind of a fun name. It means big eaters because they eat the bad bacteria.

There are also other cells, B cells, and the T cells. The T cells have this really powerful cytotoxin that they use to destroy bad cells, or cells that are infected.

Our guest today also thinks the immune system is one of the most important systems in the body. Dr. Paul Turke is a pediatrician and adjunct clinical faculty member of the Department of Pediatrics and Infectious Diseases at the University of Michigan.

He's at ASU giving a talk at the Center for Evolutionary Medicine about the human immune system and how, when and why it needs to reboot. Let me give you a hint, it's not like rebooting your home computer or smartphone.

Welcome to the show, Dr. Paul Turke, and thank you for visiting with me today.

Dr. Paul Turke: Well, you're welcome. I'm happy to be here. Thanks for inviting me.

Dr. Biology: Before we jump into rebooting our immune system, can we first talk a bit about how it works?

Dr. Paul: Sure. The immune system is a very complex part of our bodies, probably second most complex to the brain. It is that way because it has to figure out what is the body, that doesn't need to be attacked, and what is foreign, like a virus or a bacterium, that could do us harm and it does need to be attacked. That's a difficult thing to do, and so the immune system has to be pretty complicated in its structure in order to do that.

Dr. Biology: As we talked about at the beginning, there are a cast of characters, as I would call them, and these are the different cells that are part of the immune system. I talk about the macrophage and the B cells and the T cells. All of these have a very particular role.

Dr. Paul: Exactly. They do.

Dr. Biology: It sounds like a system that is pretty much perfectly worked out, so why does it need to reboot?

Dr. Paul: It is pretty much perfectly worked out, but it's not perfectly worked out. There are two general answers to that question. They're both, I think, equally important.

One is that the immune system gets old. The word for that is senescence. You have to at some point, for everything, start over. That starting over is rebooting.

But there's another angle for the immune system that you have to take into account in. That is the germs, the things that infect us, they change quickly. They evolve very quickly. You can build this great immune system that has a great memory for fighting all the usual suspects. Then time passes and the usual suspects have changed, so you have to reboot and start over.

In humans, we recombine our genes with another person. That allows us to create a huge variety of cell types to fight all these changing germs. We have to do that periodically, and we do that by making children. That's the time when the immune system basically reboots. It's when we start over again with reproduction.

Dr. Biology: The rebooting happens at birth?

Dr. Paul: Yes.

Dr. Biology: It's not something that you and I do periodically as...

Dr. Paul: Yeah. We do sort of miniature, minor rebooting in our lifetime. The immune system cells have this gene change mechanism built in. It allows them to mix things up and it gives us a good way, but a relatively limited way to produce variety to deal with the new variety that germs are always posing for us.

To really do it well, you get to a point where you have to start over. It's like you can fix your house up and add this and add that and make it better for what you need right now. But it ultimately, at some point, you got to tear down the old house and you got to build a new one. That's what we do with the immune system, and that's the most fundamental way of rebooting.

Dr. Biology: Is there an important role to the environment? For example, a lot of people hear "Nature versus nurture." In other words, you talked about the genetics, when we make babies. We're actually going to get into the genetics of rebooting your immune system.

There's another role, it seems like that once the baby's born, there is an environment they come into. The reason I'm asking this is there's a lot of discussions about allergies, in particular. A lot of babies are...Young children appear to be having more allergies. Where are we on this?

Dr. Paul: That's a great question. I'm actually going to talk a little bit about that today in another talk I'm giving. Yeah, I think that we get exposed to allergens in new and different ways than we used to in the past.

That confuses the immune system at times. It messes with what I talked about earlier, the most important thing the immune system has to do or the most fundamental thing is it has to distinguish between self and non-self.

When it comes to things like, let's say peanut allergies, a lot of children are allergic to peanuts, and they are severe allergies. You have to figure out, or the immune system needs to figure out or should figure out that peanut antigen, the proteins in peanuts, are not the enemy.

It's a process of learning tolerance. It turns out it has a lot to do with when you were developing an immune system is first exposed to peanut protein. Allergists, because it's been such a dangerous allergic reaction, they went to recommending for years now that moms who are pregnant avoid peanuts altogether.

We were told from allergists not to pick on allergies, but we were told, "Don't let kids have peanuts until they get older. Until they're two or three years old."

If you think in the broader context of the immune system, being part of an arm's raise between germs and ourselves and having to distinguish between self and non-self, there's a critical period for learning about tolerance. That critical period turns out to be when we're very young, largely when we're still a fetus inside the uterus.

When we're still a fetus, there's some special things that go on. We're protected, more or less, from outside threats. The things the immune system encounters while we're a fetus tend to be things that the immune system can count on being self. That's when the immune system learns tolerance. It learns to ignore certain things.

It's probably the exact wrong thing to do is to not give pregnant moms peanuts because when you don't do that, then the fetus doesn't get exposed to peanut antigen. Six years later, when the child gets exposed to the peanut butter or something, it recognizes as a potential foreign substance that needs to be attacked.

That's the problem. All of these can be deduced on theoretical grounds and in fact, I've been telling my patients for years, "I think it's probably safe to eat peanuts while you're pregnant."

But in 2014, at the end of the year, I think in one of the biggest and best medical journals out there, there were a couple articles published showing, in fact, that if moms ingest peanuts and peanut butter while they're pregnant, the baby that is born has a much, much, reduced chance of developing peanut allergy.

Dr. Biology: Of course this is when we're talking about the mom that does not have a peanut allergy...

Dr. Paul: That's a really astute point. In fact I have a patient who is very allergic to peanuts. His mom is very allergic to peanuts, but I didn't know that. When she's told me she was pregnant with a new baby, I said, "Oh well, you have to eat some peanut butter so that that new baby doesn't have a problem." She says, "Well, except for the fact that that would likely kill me because I have a severe peanut allergy, so that's the problem."

It's not totally a dead end there because there could be ways, in theory, of introducing peanut antigen to the fetus or the young child and avoiding exposure to mom. It'd be more difficult than simply having mom, who's pregnant to eat a peanut butter sandwich, but there's still potential ways of doing that.

Dr. Biology: If we get back to our rebooting of the immune system, there's a topic that you're going to be talking about this afternoon. I'm going to be very interested in learning more about, but if you can talk a little bit about now. It's what you call "T Cell Education."

Dr. Paul: Yeah. What happens is all your blood cells, including all your white blood cells which comprise the immune system, they get made in the bone marrow. They migrate from the bone marrow. The ones that are destined to be T cells move into the thymus. They move into there. In fact that's where they get their name – thymus begins with T, T cells.

What happens there, this is a bit of a simplification. A lot of things happen there, but sort of the main thing that happens is every young T cell has a receptor, and when it's in the thymus, it's presented with antigen. Those are proteins with shapes. If that antigen fits tightly in that T cell receptor, then the T cell in question sent signals that make it commit suicide, or apoptosis is the word.

The reason for that is the antigen you're being presented in the thymus is supposed to be self-antigen. You want to get rid of those T cells that will react to self before they get out into the periphery and can do things like attack your liver or your pancreas.

They undergo apoptosis if they bind tightly with antigens when they're presented with it in the thymus. All of that, as you probably figured out by now, depends on the thymus truly being a privileged place where only self-antigen is presented.

But remember we talked earlier about an arm's raise about germs being devious little things. If you're a germ and you want to gain free rein, you want to hide from the immune system, get yourself presented in the thymus.

What will happen then is T cells that would react to you and orchestrate an army of other cells to fight you will get deleted before they can do that. Germs have had a strong evolutionary incentive to get their antigen presented in the thymus.

Again, we go back to the best time to be assured that the antigen being presented in the thymus is truly self-antigen is, while you're a fetus, because you mom's immune system's protecting you. Along with all kinds of other things, like you're wrapped in membranes, you're inside a uterus, you're not exposed much to the outside world.

That's the time when you want to start over. You want to reboot. You want to rebuild this huge new T cell repertoire to fight things. It's the time when it's most reliably true that you're only letting T cells out that will react to foreign things, not self-things.

Dr. Biology: So there's a T cell library in there.

Dr. Paul: That's right.

Dr. Biology: All those are the good books, the good library of cells, and those are the ones that can be trusted?

Dr. Paul: The good books are the ones that don't react to self. The ones that are made to commit suicide are the ones that do react inside the thymus, and they react too strongly to self, and so they get deleted.

It's an education process is how immunologists sometimes refer to it. You go to school in the thymus as a young T cell, and you only get to graduate if you don't react to self.

Dr. Biology: Very good. Now, you're called a Darwinian pediatrician. Can you talk a bit about what that means?

Dr. Paul: Yeah. Back when what's now usually called evolutionary medicine was getting its start, one of the key papers published that is noted as the starting is one called "The Dawn of Darwinian Medicine." It was published by Randy Nesse and George Williams.

The Darwinian term got replaced with, evolutionary for a number of reasons. One is that, in some people's minds, Darwinism evokes this survival of the fittest idea, It can lead to the notion, especially when you're a pediatrician, that we're only going to take good care of the fittest children, or something like that.

Of course, it doesn't mean that at all. It means that we're using Darwinian or evolutionary principles to figure out new and better ways to take care of all children. We're not making any judgments about which ones are good, or which one should be privileged or not. We love all children, Darwinian pediatricians do, or evolutionary pediatricians do. All we're trying to do is figure out ways to better care for all of them.

Dr. Biology: Are there other doctors that call themselves Darwinian physicians? Or evolutionary physicians?

Dr. Paul: Yeah, there's a small number, but a growing number, that refer to themselves as evolution-minded or evolutionary internists, or whatever it may be. It's something that we talk about more in academic circles than we do in the clinic.

Even people that don't think evolution is a fact can benefit from, evolutionary medicine. We might think in evolutionary terms when we're trying to advise them to treat a fever, which is part of the immune system's response to help fight germs.

I don't think anybody puts a sign out on their door saying Darwinian or Evolutionary Physician because, unfortunately, half the US population would probably be turned off by that. We do proudly call ourselves Darwinian-minded, very many of us do. There's this growing, growing movement.

Randy Nesse here, at ASU, is one of the leaders of it, and has been promoting it for years and years and was one of the founders of it. I was there in the early days, too. Five or six of us used to meet once a month at the University of Michigan in the hospital and talk about this new thing and new ways we could use evolution to further medicine in general.

This was long before I was a physician, by the way. It's one of the things that led me, at the age of 39, to go to medical school. I was very much stimulated by those ideas, and it pushed me down that path.

Dr. Biology: Actually, this is very timely for you to mention that. I noted that your path of becoming a physician was a bit different than most doctors.

How did your journey in science bring you to the realization you wanted to be a doctor?

Dr. Paul: I always loved children, and I was always interested in health-related issues, but I never really wanted to be a doctor until I was doing field work in Micronesia and I met two doctors who happened to be there.

They were doing service in an underserved area in order to pay back their medical school loans. We became pretty good friends. One was from Yale, and the other one was from Penn.

I had a young daughter with us at the time. She would pick up things. I was filled with admiration because I, as an anthropologist, couldn't do all that much to help her, but they, as physicians, really could. I thought, "Wow. This is really interesting stuff."

When I got back to the University of Michigan and this evolution of medicine thing was being started up, that just furthered my interest. I eventually got to know a really smart guy named Richard Miller who was an immunologist at the University of Michigan.

He was one of the few people at the time who had an MD and was doing great work and was well-received in the field who was thinking evolutionarily. By luck, I joined with him and some of his postdocs who were also doing this. Kevin Flurkey was one that was very influential to me.

I started to get interested in the evolution of the immune system. T cells were his focus. Kevin and I, we were very interested in why the thymus is so vigorous and works so well in utero, and then starts to fade away once we're born.

By the time we're adults, there's not much left of it. From what we talked about earlier, I kind of gave that answer. The time for the thymus, when it can best do its job, is while it is at the fetal stage.

I decided at that point, from working in Rich's lab, after learning some immunology, that I really liked this stuff. I decided I was going to go to medical school, but not to be a practicing physician, but just to get the MD so that I would have some chance of being hired in a microbiology or pathology department of some university.

When I got there, you do a lot of patient stuff in medical school, and I found out that I really liked treating and interacting with the kids.

In the end, I ended up pretty much as far away from joining an immunology lab somewhere and not seeing patients and just being in academia. I ended up opening a private clinic where I could work with kids and try to use my evolutionary and anthropological background to help everyday kids coming in with their moms and dads.

Who have their runny noses and their fevers and their ear infections, and so on, and to use evolutionary principles to figure out new and better ways to treat them, to tweak things, really.

I don't want to make it sound like it's revolutionary if you understand evolution, oh you can fix everything. It's not that, but there are little things, subtle things, and some not so subtle things that you can do if you have evolution in mind when you're running a community pediatric practice.

Dr. Biology: How does anthropology fit into the practice of medicine.

Dr. Paul: Well, in pediatrics, it teaches that there are lots of ways to raise healthy happy children, and so it allows me, as a pediatrician, to be more flexible than some of the old-fashioned pediatricians who used to say, "No, you have to do it this way. You have to throw away the bottles when they're 12 months old. You have to have them sleep in this condition or this environment, and not that condition."

Once you're an anthropologist, you know there's lots of ways of doing things. There's lots of good ways of doing things, and you can be more flexible. I think that is something that parents like, especially in this day and age where we've got an Internet and they can Google how people do it in different places. They want to talk about it, and I have some experience in that because that's what I studied as an anthropologist, child-rearing.

Dr. Biology: Back to the evolutionary medicine and the Darwinian pediatrician. Are there misconceptions about the difference between someone who says that they're going to practice with a focus on evolutionary medicine and a traditional pediatrician?

Dr. Paul: There are. I really had a wake-up call when I had an interview with the "New Scientist" magazine. I didn't write the headline, of course, but the headline was something like, "Darwinian Pediatrician says Hold the Painkillers."

I generally support that, in the sense that acetaminophen and ibuprofen, millions and millions of doses of that are taken every year, not just in adults, but in children. Those are great medicines when they're called for. My point was that they're used too much. A lot of the things they're used for...

When you get a twisted ankle, say, it hurts, so the pain makes you lay off, and not keep playing that soccer game. It's not all bad for a twisted ankle to hurt. The swelling and the inflammation that occurs when you twist your ankle, those are all part of the immune system and the inflammatory system working to heal that ankle. When you take some of these powerful anti-inflammatory medicines just willy-nilly, you can be interfering with all that and causing more harm than good.

I said that very briefly. It was a one-page article, and I was shocked to see a few days later, after it came out, some comments of people. There was somebody who said, "I had back surgery the other day. Would Dr. Turke, a Darwinian doctor, want me to have had that surgery without anesthesia? Would he have wanted me to not take any painkillers afterward?"

There were other people who said, "Well, I'm glad he's not my pediatrician. That's cruel to hold the painkillers." Well, of course, that's not what I was saying at all. That was a wake-up call to me because you have to always keep in mind when you're saying things what people will read into it.

All I was saying is that if you're son or daughter twists an ankle in a soccer game, bring her to the sideline. Let her sit down. As long as she's comfortable, let her rest it. If she can keep it comfortable by just taking it easy, that's the best way to let it heal. Let nature take its course.

If a child can't get comfortable, is writhing on the bench because they're in pain, then you go the emergency room and then you may need some painkillers. It's a little bit of a balancing act.

Again, I think it's this term, Darwinian, survival of the fittest. It's this harsh nature, red, and tooth and claw kind of idea. It's not that at all. Darwinian pediatrics, or evolutionary pediatrics, I think is the kindest pediatrics.

Dr. Biology: I would sum it up as listening to the body.

Dr. Paul: Yeah, right.

Dr. Biology: What is it telling you, and paying attention, so that you're not doing what it's telling you not to do.

Dr. Paul: Exactly.

Dr. Biology: Sports play such a huge role in our lives. It's not that sports are bad, it's just that big game sports, one of the things that comes to mind are steroids, in particular, the players that are taking steroids, because they have an inflammation, and that way they can go play. The problem is what's happening down the road?

That's another example of taking it too far, trying to avoid what the body is trying to tell you.

Dr. Paul: Yeah. That's very dangerous. It's funny because I kid with some of my athletes, they're high school kids that come into the office. They're dreaming big. They're thinking they're going to be the next guy signing a contract, or next woman signing a contract for a million dollars, or whatever it is.

If I'm a little suspicious that they might be taking some performance enhancing drugs, or more commonly, if they just want to get back into the game before they heal, and they shouldn't, I'll joke with them and say, "So, what are you getting paid for next Saturday's game? $100,000? $200,000?" "No, no, no. We're getting paid nothing."

If you want to be healthy over the long term, you don't want to be messing with things. You want to let your body heal if it's injured. You certainly don't want to be taking any drugs that over the long run are going to harm you.

Then again, if they're receptive to it, I might point out that if having more steroids in our body, or more testosterone in our body, were good for us overall, we would have evolved to have that. You've got to be very careful with all that stuff.

Dr. Biology: On "Ask a Biologist" I have a history of asking three questions of all my guests. No one gets out without these three questions. We'll start off.

When did you first know you wanted to be a scientist? In your case, later, where was the particular moment when you knew you wanted to be a physician?

Dr. Paul: The scientist thing came way earlier. I was born in '53, so there was Sputnik, and then the US Space Program, and all that. When I was about three years old, I wanted to be an astronaut.

Then, after thinking about, "Yeah, that's just kind of like driving a bus," I wanted to be the guy who figures out how rockets work and physics, and all that. That was the first thing that I loved as a kid.

Then I got into dinosaurs. I learned evolution early and became more interested in biology than anything else and evolutionary theory. It wasn't until we had our first child and I met these doctors, Yap is the island we were on, that I realized I really did have a big interest in medicine, pediatrics in particular. I was about 32, I think, when I first decided, "Yeah, maybe I should think about going to medical school."

Dr. Biology: For our next question, I take this all away from you. You don't get to be a scientist. You don't get to be a physician. The question is what would you be, or would you do?

Dr. Paul: That's easy. Back when I was making the decision to go to medical school, I had a sign on my door. I think my wife put it up there because we talked about it. It was called "Salsa Farmer." I was going to make organic salsas, locally produced, and so on. This was way ahead of the locavore movement. I would have been a salsa farmer.

Dr. Biology: Oh, a salsa farmer, interesting. I always say that our farmers, in many ways, they're scientists themselves.

Dr. Paul: Yes.

Dr. Biology: The final question is, what advice would you have for a young, budding biologist, or perhaps someone who wants to change careers?

Dr. Paul: I would say it's never too late. You can always do it. It's a little easier to go to medical school when you're a little younger than 39, but I've known people older than me that have done it. It's never too late to do that.

I would say to young biologists to stay curious. Keep an open mind. Get out there in nature and see things. I would encourage them to think big.

Too many people, down the road, your Department Chair or your 10-year committee, or your grant panel, NIH or whatever, who's forcing you to be narrow, so while you can be free and think about everything, think about everything.

Dr. Biology: This leads me into some research I did on you. I found you are writing a book.

Dr. Paul: Yes.

Dr. Biology: The title is "Bringing Up Baby: An Evolutionary View of Pediatrics."

Dr. Paul: Correct.

Dr. Biology: The first sample chapter is on the Web, so I was able to have it for one of my evening readings. I found it really enjoyable.

Dr. Paul: Thank you.

Dr. Biology: I wondered if there was a section that we could have you read. Because we've talked about changing careers, I think there's a place in there that would fit very nicely for that.

Dr. Paul: Sure. The subsection is, I call it "A Tortuous Journey." It starts off, At age 39, I went to medical school. I got there by a circuitous route, with stops along the way in anthropology, evolutionary biology, and immunology.

The more typical route is straight and narrow and littered with multiple-choice exams. Exams and more exams, from high school to retirement, they validate every doctor's career. Personally, I don't think much of exams. They conflate factual recall with understanding.

I'm not sure why I was let in, and I hope this book doesn't trigger an investigation. It's quite possible, though, that someone with a name similar to mine got an undeserved rejection letter. I entertain this suspicion because an informant, a doctor friend on the Faculty of one of the two medical schools to which I applied, explained how the selection process had proceeded at his institution.

My Ph.D. in anthropology, the articles I'd published, the classes I'd taught, letters of recommendations from colleagues, none of them mattered. Four thousand applications were plopped on a secretary's desk, and she was instructed to send rejections to all but the top ten percent, judged solely on the basis of undergraduate grade point average and Medical College Aptitude Test score. The remaining applicants were granted interviews, and I was, mysteriously among them.

I left mine feeling as though I'd been hazed. Not the tame kind of hazing that occurs at college fraternities, where mortality rates are fairly low, but more like the hazing that elders have committed on adolescents, throughout much of the world, over much of human evolutionary history.

Anthropologists refer to these affairs as "Rites of passage," which is an overly dignified label for ceremonies that generally include septic circumcisions.

My interviewer was a 60-something female pediatrician who looked kindly enough but wasn't. Pleasant conversation was not her forte. As an icebreaker, I mentioned that it was a nice day, adding that we nevertheless needed rain. Her response was to ask whether I was interested in medicine or meteorology.

Things deteriorated from there, and I soon found myself scanning the room, hoping not to spy any dirty scalpels. She was unimpressed with my background and quite concerned that my interest in certain theoretical issues would interfere with the care of patients. Her disdain for theory surprised me because she was employed by one of the largest and most highly regarded research hospitals in the country.

Moments later she closed our session with a question, muttering as she got up to leave, "Are you incapable of giving a concise answer to a question?" My quick reply was, "No, which" And I resisted rubbing this in, is pretty concise.

Dr. Biology: [laughs] Very good. Paul Turke, I want to thank you for visiting with me.

Dr. Paul: My pleasure.

Dr. Biology: You've been listening to "Ask A Biologist," and my guest has been Dr. Paul Turke, pediatrician and adjunct clinical faculty member of the Department of Pediatrics and Infectious Diseases at the University of Michigan.

If you want to learn more about the immune system, we have our comic book, "Viral Attack" ready for you at any time – just pop on over. The address is askabiologist.asu.edu/viral-attack or you can just Google the words "Viral Attack." We'll be a top result.

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Remember, even though our program is not broadcast live, you can still send us your questions about biology using our companion website. The address is askabiologist.asu.edu or you can just Google the words "Ask a biologist." I'm Dr. Biology.

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