



Dr. David Stukus: Hello, and welcome to "Conversations from the World of Allergy", a podcast produced by the American Academy of Allergy, Asthma & Immunology. I'm your host, Dave Stukus. I'm a board-certified allergist and immunologist, and serve as a social media and medical editor for the academy. Our podcast series will use different formats to interview thought leaders from the world of allergy and immunology. This podcast is not intended to provide any individual medical advice to our listeners. We do hope that our conversations provide evidence-based information. Any questions pertaining to one's own health should always be discussed with their personal physician. The Find an Allergist <http://allergist.aaaai.org/find/> search engine on the academy website is a useful tool to locate a listing of board-certified allergists in your area. Finally, use of this audio program is subject to the American Academy of Allergy, Asthma & Immunology terms of use agreement which you can find at <http://www.AAAAI.org>. Today's addition of our conversations from the "World of Allergy" podcast series, is our first installment where we interview a researcher about a specific study that was published. We are extremely pleased to welcome Dr. Elina Jerschow, who is an Associate Professor of Medicine at the Albert Einstein College of Medicine in Montefiore Hospital in New York. Dr. Jerschow's research interests focus on the pathogenesis of drug allergies and improving our understanding of diagnostic and therapeutic approaches to these conditions. Dr. Jerschow has over 35 peer-reviewed publications, and today we are going to focus on one of her most recent studies titled "Safety and Outcomes of Oral Graded Challenges to Amoxicillin without Prior Skin Testing," which was published in the January 2019 issue of "*Journal of Allergy and Clinical Immunology: in Practice*." Dr. Jerschow, thank you so much for taking the time to join us today and welcome to the show.

Dr. Elina Jerschow: Thank you very much for inviting me, and I'm happy to join.

Dr. David Stukus: Great. Well, before we get into some details about your study, you have a long and remarkable career dedicated to research as well as patient care. Would you be willing to share with our listeners the aspects of research that you find most exciting?

Dr. Elina Jerschow: Thank you for asking that. I feel that the most exciting part of research and clinic is the fact that they help each other. I think whatever we learn in clinic, it benefits research, and whatever we learn in research, it benefits clinical work. Indeed, it's a challenge to find the balance between the two. I feel very fortunate we have an environment where this was possible. It has allowed me to do both, and certain environments it's very important to force the research of an institution, and of course there are always challenges to find time to do both, but I feel the benefit of doing both is actually so great that it should be possible for anyone who wants to do it.

Dr. David Stukus: Well, that's great. You're clearly very passionate about it and I know that we are all benefiting from the great work that you're doing.

Dr. Elina Jerschow: Thank you.

Dr. David Stukus: Now, can you tell us why you decided to conduct this particular research study?

Dr. Elina Jerschow: So before that study that was just published, we had another study, which was published I think about a year or two ago. That was a study on penicillin testing and challenges in patients who are coming from our minority background. So most of the patients were from Latino or African-American background in The Bronx, New York, and unlike the latest study that we are going to talk about today, this first study was focused on skin testing and then challenges. So while doing this study, and skin testing all the patients who were willing to join our research, we've noticed that some of the patients had positive skin tests, and we would tell them that unfortunately they're really allergic to penicillin and they should not undergo a penicillin challenge, and then I had a family of two Irish women, a mother and daughter, who were very fair-skinned, and they had a positive skin test, and I told them both, "It's very interesting. It seems to run in the family, because you clearly have a positive skin test, and we shouldn't do a penicillin challenge." But both of them were highly motivated and they said, "Why not?" They said, "We didn't die back then."

Dr. Elina Jerschow: "So why don't we try again now?" and their reaction was literally many years ago and so after discussing the risks and benefits we decided to proceed with the challenge, and we did the challenge on both of them and both of them passed the challenge without any single adverse reaction. So moreover, these two patients actually needed penicillin. That's I think why the motivation was there. They both completed a course of Augmentin of 10 to 14 days each, and they had no problems. So that made me think that maybe penicillin skin testing could indeed be false positive, as it is also stated on the label, that there are possible false positive reactions to PRE-PEN, for example, and I thought by just not challenging patients with history, like my patients wisely pointed out, their reaction in the past was not life-threatening. So by not-- by doing skin test that may be false positive, we might deprive patients who are actually not allergic from the chance of having penicillin for their treatment. At this point, we thought maybe it would be a good idea not to do skin testing in patients who don't have history of life-threatening reactions to penicillin. So that's how it came about.

Dr. David Stukus: Well, that's really fascinating. So you took your experience as a clinician to really start to generate some new questions and then you conducted a research study to try to answer those. That's amazing.

Dr. Elina Jerschow: Yeah, I was highly motivated by my patients, so it's--

Dr. David Stukus: <laughs>

Dr. Elina Jerschow: I need to thank them, and actually, I did.

Dr. David Stukus: Ah, excellent.

Dr. Elina Jerschow: Yeah. Yeah.

Dr. David Stukus: So before we get into this recent study that you published, can you just touch upon some of the more cumbersome aspects of trying to clarify somebody with a self-reported penicillin allergy? So what are some of the challenges that we all face in practice?

Dr. Elina Jerschow: Good question. I think there are a couple. One challenge I feel that has been well-presented by Roland Solensky on the past, during the past academy meeting, where he said, "In United States we have about 6,000 penicillin allergic patients for each allergist in the country." So I found this arithmetic quite fascinating. That means if I personally see, I don't know, I'm just making an estimate, let's say, 500 patients, new patients a year, it would take me about 12 years to skin test my portion of penicillin allergic patients, and I would have to give up all other patients that come to see me for other reasons, like let's say asthma or ARD. So that will be quite a journey, and I think this is one of the challenges we all face. I feel that maybe just like we are dealing with diabetes or high blood pressure, when people have the condition, like diabetes or blood pressure, hypertension, so they don't have to always see cardiologist or endocrinologist. They might be well managed by their primary care practitioners, and I think penicillin allergies might consider, or handling penicillin allergy might be possible by primary care physicians as well. So I think by empowering primary care physicians to evaluate penicillin allergy and in patients who didn't have life-threatening reactions and administering challenge in primary care setting should be an option, and hopefully that will be an option at some point and that will relieve the burden of all allergists in United States and probably around the world because it's not just United States problems, it's a problem that has been reported from many different countries as well. So by letting other physicians to partake their-- or to be able to evaluate patients for a penicillin allergy, we might be able to actually relieve the epidemics of penicillin allergy. That's number one. Number two, I feel that patients sometimes are deterred by the multitude of steps that are currently present as a barrier to being evaluated for penicillin allergy. For example, if, let's say, I am penicillin allergic and I decide to investigate further. So I would probably need to go to see my primary care physician first, ask for a referral to see an allergist. Then I go to an allergist's office. Then the allergist is possibly having PRE-PEN in his office but maybe not necessarily Pen G, which is the second part of the skin testing regimen, and the allergist in that case might say, "Look. I am happy to see you for a follow-up to do the skin test," and the skin test, the visit probably involves about anywhere from 30 to 60 minutes. So a patient who comes again for skin testing will need to spend another hour of his or her busy schedule to do penicillin testing, and then there is also a challenge that may be conducted immediately after skin testing or if the allergy practices wait to visit or if the person has something else scheduled. Then it's not going to be possible that day, so they might actually need to come back again. So we are looking into about a total of three to four visits I don't think people have that much time, and when I did skin testing study, I realized that more than half of the patients did not have time to stay for a challenge or return for a challenge. So I think this is really the challenges that we face in practice right now and hopefully by working on this together we might be able to suggest a different strategy.

Dr. David Stukus: Yeah. I agree 100 percent and, you know, if we think of the sheer number of patients with self-reported penicillin allergy, if we're going to have any hope of making a dent in that and clarifying, we need to really think outside the box and think on levels of widespread implementation.

Dr. Elina Jerschow: Yeah. I agree.

Dr. David Stukus: Yeah.

Dr. Elina Jerschow: I agree, yeah.

Dr. David Stukus: Well, so that gets us to your study. Can you tell us about your study design and focusing on what the primary outcome was that you looked for?

Dr. Elina Jerschow: Sure. So our study design was fairly simple. We included all patients who reported penicillin allergy. We screened them and then we excluded those who reported life-threatening reactions. So life-threatening reactions could have been anaphylaxis requiring intubation. Also when anaphylaxis was severe but not required intubation but the patient was exposed to several medications at the same time. For example, such as an anesthesia setting. Those patients were excluded as well, and then we excluded patients with delayed life-threatening reactions, such as Stevens-Johnson or DRESS. So that left us with 155 patients for the study. I'm sorry, 159, and all of these patients were offered to have a challenge, direct challenge, without skin testing. So that was our study design, and the primary outcome was the tolerance of the penicillin challenge. We used amoxicillin, and why did we use amoxicillin? I think there are a couple of reasons to this as well. So first of all, it's one of the more common-prescribed oral penicillins. Secondly, it has another advantage. It's the same as synthetic penicillin, so it's covering both, plain penicillin, as well as a penicillin with a side chain. There was a study, I believe, around 2010 that indicated that about five percent of patients are not being identified as penicillin allergic if they're not tested with amoxicillin. So in order to make sure that we cover all the bases and all patients can tolerate not only plain penicillin but also penicillin with a side chain, we decided to use amoxicillin, and I think that was the reason for amoxicillin. Also it's very easy to use in clinic. It's a suspension that we use. We had placebo, which was also more or less like a suspension syrup. So it's the same syrup as people use in pharmacists who prepare suspension of medications for children. That was our placebo, and then we administered a basically two-step challenge but three-step, because we also used placebo. So placebo and then one-tenth of the medication, and then the full dose of the medicine, which was 500 milligrams for adult patients. Our study included children the age of seven and above as well. So for children it was dependent on the child's age and weight, so-- and then we administered placebo and the medications and observed the patients for a total of about one and a half hours. Maybe more like 1 hour, 45 minutes, I think, and then we told the patients who passed the challenge that they should be able to tolerate penicillin in the future. We told them that the testing was specifically throughout anaphylactic type of reactions, more like of an immediate type, and unfortunately that does not exclude reactions that could happen after three or five days of being on antibiotics, penicillin antibiotics. But in that case, we advised them should they need penicillin they would take it, and should they have any problems they should stop the medicine and give us a call. So that's how we approached the challenge. That make sense?

Dr. David Stukus: Oh, absolutely. So it sounds like just to summarize, and correct me if I miss anything, you took a group of patients who all shared the same history of having non-life-threatening reactions to penicillin antibiotics at some point in the past, and all of them were above the age of seven. So older children and adults, and essentially you just gave them a placebo, followed by a 10 percent dose of amoxicillin and then a 500-milligram dose and then watched them for a little while; does that sound about right?

Dr. Elina Jerschow: Correct. Yes, yes, absolutely.

Dr. David Stukus: Okay.

Dr. Elina Jerschow: Thank you for summarizing.

Dr. David Stukus: Oh, no. Thank you. Yeah, so-- and it sounds like there was no skin testing involved; is that correct?

Dr. Elina Jerschow: Yes. There was no skin testing.

Dr. David Stukus: Okay. Well, what did you find?

Dr. Elina Jerschow: Well, we found that most people are not allergic to penicillin. In fact, we had four patients who reported allergic reactions. One was subjective, so the person was very itchy and couldn't stop scratching, and it really continued over one hour, and so we decided to call him allergic and we-- and he reacted actually to the last dose. With the first dose of amoxicillin he had slightly-- some slight itch that he wasn't really concerned about, so we gave him a second dose, and then the itch aggravated by so much that we had to treat him actually in clinic. So there were no objective signs of reaction in that patient, but because of unresolved symptoms, we called being allergic. The other three patients had reactions with skin rash, so all of the rashes were delayed. All of the rashes happened after they left the office, either the same day in a few hours or the next day, and we offered treatment to all of the patients so they all contacted us or their physician. For one patient it was her physician, and they called us and they told us about it. None of the patients actually took the treatment because the rash resolved continuously, but in that case we told them not to take penicillin, and two of the patients I actually saw and they did have rashes. Either the rash when it happened or the pictures, so it was quite reliable in terms of being reactive to penicillin. So we advised them not to take penicillin in the future. But the rest of the patients were able to tolerate challenges, and many of them continued taking penicillin for different reasons and they were able to tolerate as well.

Dr. David Stukus: So out of 159 patients, was it only four that had objective symptoms and all of them were mild, non-anaphylactic; is that correct?

Dr. Elina Jerschow: Correct, correct. We actually-- 3 patients did not complete the challenge or 4 patients, so we counted as 4 out of 165, which brings us down to 2.6 percent of all patients that had been challenged properly did not have allergic-- actually have allergic reactions, yeah, so 2.6 percent.

Dr. David Stukus: Wow.

Dr. Elina Jerschow: Yeah.

Dr. David Stukus: So 97 percent of the people in your study had been avoiding penicillin antibiotics for years and yet they were--

Dr. Elina Jerschow: Correct. Yes.

Dr. David Stukus: --fine with it.

Dr. Elina Jerschow: Yes.

Dr. David Stukus: That's amazing. Now, I have a unique question to ask, because there's a aspect of your study that I just find truly interesting. Can you tell us a little bit about those patients that had symptoms after the placebo dose?

Dr. Elina Jerschow: Yes. We found it fascinating as well. Thank you for asking. Yeah. Many patients had reactions, kind of a placebo type of reaction. So we calculated that we had 20 percent of reactions that were non-allergic in nature to either placebo or amoxicillin. Those reactions were fairly common actually in both studies. The one that I described before with skin testing, during the challenge people still had a lot of reactions, and also during this study we had quite a few patients who reacted to placebo, and placebo reactions were very common in-- actually, interestingly enough, some of them were very objective, such as urticaria, but it happened in patients who had history of chronic urticaria, for the most part, and I, you know, I'm not sure how to explain that. Could it be a bout of chronic urticaria during the challenge? It's possible. Is it that there was some component of being anxious about the challenge and maybe that triggered the reaction? It's possible. We're not sure. We also had patients who reacted with a itch that resolved continuously and then nausea. Some of the patients had nausea, vomiting, diarrhea. Definitely a lot of itchy mouths and palpitations. So quite a few different reactions to placebo. That being said, I know there is a very good study from Boston where they observed no reactions to placebo, where they also used placebo, and the setting was very different. So the Boston study was conducted within a hospital while our study was in outpatient clinic, and the hospital patients were mostly motivated to get the right treatment, so I'm not sure if the motivation causes different response to placebo or medication in people, so that's my speculation, but of course I wouldn't know for sure.

Dr. David Stukus: Well, it's really interesting, and you know, personally, I take that as something for allergists or any medical professionals who would conduct a challenge to provide that anticipatory guidance heading in and letting patients know that they may feel certain subjective symptoms.

Dr. Elina Jerschow: Yeah.

Dr. David Stukus: But we need to be very careful and assess objectively to see if any type of reaction's occurring.

Dr. Elina Jerschow: Correct. Yes, I agree.

Dr. David Stukus: Well, so overall, it sounds like you found it to be very safe and effective to forego skin testing and administer amoxicillin to patients who all had a history that was not worrisome for prior severe life-threatening reactions to penicillin. Now, do you think we should be doing this in clinical practice?

Dr. Elina Jerschow: Yes, I think so. We continue to implement this approach in our clinical practice now, so we have continued conducting challenges this way. In patients who don't have history of life-threatening reactions, we actually administer challenge, and in patients who do have life-threatening reaction history, especially the immediate type, we do skin testing first. But I think it will simplify a lot of things in the clinic when we're able to conduct direct challenges, and our study's not unique. So I really like the Canadian study from JAMA I think it's 2017 (note: 2016), where about 800 children were challenged to amoxicillin soon after they had reactions, so within several weeks to several months, and more than 90 percent of children passed the challenge without having any problems. So I feel that actually kind of confirms our suspicion that many of these reactions are possibly due to interaction between the antibiotic and the infection, or maybe sometimes they're purely infectious rashes. But then the child who hasn't been challenged by Canadians in that study, would carry the label of being allergic until late in life, and that will probably continue with such epidemics of penicillin allergic people. So I think doing direct challenges is a good idea, as long as you select patients appropriately.

Dr. David Stukus: Mm. No, and I agree 100 percent, and that's something we've been doing at our institution as well. Now--

Dr. Elina Jerschow: Oh, you have been? That's great.

Dr. David Stukus: Yes, yes, and I think, you know, with your research, as you mentioned, it's contributing to a body of literature now that's all showing if you select patients appropriately through their history and you select those that have a benign history of prior reactions or it's been an extended period of time, that this is something that we can be doing.

Dr. Elina Jerschow: Right, right.

Dr. David Stukus: Now, do you have any tips for physicians, and even patients who may be listening, to help determine if prior symptoms while taking penicillin were truly due to an allergic reaction?

Dr. Elina Jerschow: Well, all I can say is let's find out for sure, because people who are labeled penicillin allergic tend to be treated with different antibiotics that frequently are suboptimal to penicillin. Penicillin is our oldest antibiotic. It's going to be-- I believe it's going to be 91 this year. It's quite old, and it's still one of the most effective and the most helpful antibiotics we have. So I think being able to take penicillin and avoid side effects that are sometimes associated with newer antibiotics is a great idea, so it's actually really helping the patients and the physicians in treatment of many different conditions. So I think finding out for sure it a great idea to do so.

Dr. David Stukus: I love the positive message. Thank you.

Dr. Elina Jerschow: Thank you.

Dr. David Stukus: So now that this project is published, and I know that it was completed a long time ago and the lag between that and, you know, publication status, but can you tell us a little bit about what you're focusing on now?

Dr. Elina Jerschow: Thank you for asking. So right now I know in our hospital there's a lot of interest in antibiotic stewardship, and there is a suggestion of actually known allergists conducting challenges in patients who are at this time admitted as inpatients. So from surgical side as well as from medicine side, we are planning to conduct challenges directly after evaluating patients and appropriately selecting the patients for penicillin challenges directly. So that brings us to my initial comment that it would be nice if penicillin allergy could be evaluated by known allergists as well, and hopefully that will give us some fruition and hopefully we'll get some results from that study as well. It's very early, but I'm sure a lot of other people conduct similar studies around the country and maybe outside of the United States, so I'm kind of expecting a body of evidence coming at us with safety data on conducting penicillin challenges by known allergists.

Dr. David Stukus: Well, that's great. I can't wait to see the results of your study, and I just-- I'm a big fan of the work that you're doing, so thank you for all of that.

Dr. Elina Jerschow: Thank you very much. Thank you.

Dr. David Stukus: Well, thank you again for taking the time to be with us today. I think this was a great conversation, and I personally love hearing some of the aspects of your personal career and experiences that led you to conduct this study, and we appreciate you taking the time to share with us why and what you found. So before we conclude, is there anything else that you'd like to add?

Dr. Elina Jerschow: No. Thank you very much for inviting me. It was a great honor and a pleasure to be with you today, and I hope it was useful to our listeners.

Dr. Davis Stukus: Thank you for mentioning that, and as you mentioned, it's really hot off the press at the time that we're recording this, and we will be able to put that as a link in our show notes. That's great. We hope you enjoyed listening to today's episode. Please visit <http://www.AAAAI.org> for show notes and any pertinent links from today's conversation. If you like the show, please take a moment to subscribe to our podcast through iTunes or Google play so that you can receive new episodes in the future. Thank you, again, for listening.