Dr. Mariam Hanna
Hello, I'm Dr. Mariam Hanna and this is The Allergist, a show that separates myth from medicine, deciphering allergies and understanding the immune system.

The baby has eczema. Oh mom, did you try eliminating milk from your diet? Baby crying?

He's hungry. Maybe baby needs to be fed? Your kid has allergies? Did you eat clean during your pregnancy?

People, can we please just stop that? Let's face it, pregnancy is already a circus of symptoms.

Nausea, cravings, fatigue, unsolicited advice from strangers. Because if there's one thing that's more unpredictable than third trimester cravings, it's how the immune system behaves during those nine months and beyond. So in this episode, we're reviewing the evidence, busting a few myths, and talking practical management of allergic conditions during pregnancy, from rhinitis and asthma to drug allergies and anaphylaxis.

We'll also touch on fetal risks, maternal safety, and how do we navigate the grey zone where better safe than sorry starts causing more confusion than clarity. We're diving into all the juicy and slightly stuffy details. Too soon for a joke about pregnancy?

Never mind. Alright, alright, then allow me to introduce today's guest who took me up on this wonderful topic. Dr. Lana Rosenfield is an assistant professor at the University of Manitoba in the section of allergy and clinical immunology. She completed her medical training and internal medicine residency at the University of Manitoba, followed by a clinical immunology and allergy residency at McMaster. She currently practices at the Winnipeg Clinic. Dr. Rosenfield, thank you so much for joining us today and welcome to the podcast.

Dr. Lana Rosenfield
Thank you so much for having me.

Dr. Mariam Hanna
Alright, I'm really excited that you actually agreed. Let's start off with giving us an overview of how pregnancy might alter the maternal immune system and how this might change some of the allergic or atopic conditions that we see.

Dr. Lana Rosenfield
So when it comes to allergic disease, the hormonal changes in pregnancy can definitely have multiple effects. One of the most important ones is there is a shift from Th1 to Th2 disease in patients who are pregnant, and of course this can increase to increased allergic inflammation because of increase of IL-4, 5, and 13. We also see some decreased cell-mediated immunity in pregnancy due to these hormonal shifts, and especially in asthma patients, the risk is that this can lead to increased infections, which can lead to asthma exacerbations, which can have poor outcomes in pregnancy as well.

We also know that pregnancy- associated hormones can also have effect on nasal blood flow, mucous gland production, so these can all affect patients who have various atopic diseases such as rhinitis and can worsen symptoms during pregnancy.

Dr. Mariam Hanna
So it's a disaster essentially on multiple fronts. Definitely Th2 heavy and then cell-mediated immunity being compromised, infections being big triggers for some of these conditions to flare up. Okay, the perfect storm.

So we're going to start with allergic rhinitis and we will touch on asthma and other conditions, but let's start there. How does allergic rhinitis typically behave during pregnancy?

Dr. Lana Rosenfield
So as we will talk about with all of most of these allergic conditions, they may worsen, they may improve, or they might not change at all, and it really is patient-dependent.

Dr. Mariam Hanna
Okay, so there's no slam-dunk answer. It just sounds like most of the questions that I answer in clinic. Okay, so what are the safest treatment options for somebody that has more active allergic rhinitis during pregnancy or during breastfeeding?

Are there safe options that we can talk to our patients about?

Dr. Lana Rosenfield
So the safest options of course are going to be your non-pharmacologic therapies. So avoidance of allergen triggers and non-medical therapies such as nasal saline rinses will be your safe option because there is actually no medication involved in these therapies. When it comes to more milder symptoms, intermittent symptoms, it is safe to use second-generation antihistamines such as loratadine, cetirizine, which are both Category B and are safe in pregnancy.

If symptoms are more severe, then we would consider using nasal steroids. Typically, we would use the lowest effective dose that we can, and we know that budesonide, fluticasone, memedazone are all safe to use in pregnancy, but when we talk about medications in pregnancy, we'll talk about a lot of this in the next little bit, but the lowest effective dose is always which we're going to aim for when we are using medications. There are some that aren't as safe in pregnancy, so there isn't data on nasal antihistamines, so typically we will try and avoid those in pregnancy as well as decongestants, which we do prefer to not use even outside of pregnancy, but in pregnancy there is known congenital anomalies that can happen, so we want to try and avoid that if possible.

Montelukast is also safe in pregnancy, Category B, and can be used if patients do have benefit from this.

Dr. Mariam Hanna
Okay, perfect, and just for the sake of people that don't talk about these different categories routinely, what do we mean by saying Category B medication?

Dr. Lana Rosenfield
So, Category B is going to be when we talk about medications in pregnancy, graded A, B, C, and so on, of what the evidence is out there for safety. Really, it's impossible these days to get a Category A safety measure, which would be the best because we're not doing randomized control trials in patients that are pregnant, but Category B is going to be that highest level of safety that we're going to be able to get in data these days.

Dr. Mariam Hanna
Okay, so highest level of safety without it being a randomized control trial and no evidence of something horrible happening.

Dr. Lana Rosenfield
Exactly.

Dr. Mariam Hanna
That people have used it. Okay, let's move on to asthma, which represents really one of the most common chronic conditions that people can go into pregnancy having. How should our asthmatic moms be monitored and how do we manage their asthma control during pregnancy?

Dr. Lana Rosenfield
So, it is important to monitor these patients more closely because there is risks with having poorly controlled asthma and asthma exacerbations for adverse perinatal outcomes. So, generally, the GINA guidelines do recommend monitoring about every four to six weeks throughout pregnancy to make sure that patients do have symptoms controlled and trying to prevent exacerbations.

Dr. Mariam Hanna
Okay, so GINA, meaning like we're just asking them the same questions that we would ask any of our asthma patients on follow-up visits, just to make sure daytime symptoms, nighttime symptoms, activity, and usage of breakthrough medications. Is that correct?

Dr. Lana Rosenfield
Yeah. Spirometry, follow-up spirometry is safe to do in pregnancy. You wouldn't do bronchoprovocation testing in pregnancy, but it is safe to do spirometry if you want to monitor lung function as well.

Dr. Mariam Hanna
Okay, and many of our mild asthmatics and beyond are on some kind of maintenance inhaler or controller therapies. Are there ones that would be more preferred over others?

Dr. Lana Rosenfield
So, for maintenance therapy, so inhaled corticosteroids for the most part are going to be safe to use in pregnancy. Generally preferred ones are budesonide, beclomethasone, fluticasone, but if they're on an alternative one prior to pregnancy, it can be continued. Just the most safety data is on those three.

Lung agonists also have been shown to be safe in pregnancy, so salmeterol and formoterol can both be continued. When it comes to anticholinergics, those ones do have more minimal data and don't have as much of a safety record as we have with inhaled corticosteroids and with the LABAs. And like I said previously with rhinitis, montelukast is category B.

It can be continued in pregnancy.

Dr. Mariam Hanna
Okay, and that's really good to hear about LABAs because the new GINA guidelines as well as CTS, increasingly we're using kind of maintenance and reliever therapies in these patients with LABAs included in there. So, good to know that that's fine. Atopic dermatitis will be the next one that I'm itching to talk to you about.

Eczema can be influenced, as we know, by hormonal changes or fluctuations. What are common changes that we see in patients with atopic dermatitis? Are you going to tell me the same answer?

Dr. Lana Rosenfield
I will. So, same with rhinitis and asthma. Atopic dermatitis can worsen, improve, or not change.

One thing to note though, I think it's important with atopic dermatitis, there are a lot of kind of mimickers that can occur in pregnancy. So, if patients are having worsening symptoms, it's important to think, is this worsening of eczema or is this another pregnancy condition that can cause pruritus or rash that's different from atopic dermatitis? So, to making sure to rule out those other conditions such as prurigo of pregnancy or cholestasis of pregnancy.

Dr. Mariam Hanna
Right, one of them being a more emergent thing to address. Okay, what topical therapies are considered safe? We have new generation topical therapies and then we also have systemic treatments for atopic dermatitis as this area has exploded in the past five years.

What's category B or better, should I say?

Dr. Lana Rosenfield
So, topical corticosteroids are considered safe in pregnancy for the most part. There is some possibility of systemic absorption though, so really what you want to try and do is use the least

potent dose. Try and use, if you do need to use higher potency, use it in the smallest area possible, but it is important to use them if it is required.

When it comes to other topicals like topical calcineurin inhibitors, really, there isn't a lot of data and it would be something we probably would avoid if we can. Other topicals or even oral, when we talk about JAK inhibitors, they actually wouldn't be used in pregnancy just due to lack of data at this time. So, the topical corticosteroids are really going to be the main topical therapy in pregnancy.

Of course, always considering your non-medical approach with avoiding any known triggers or even UVB therapy is okay to continue during pregnancy. When it comes to some of the systemic therapies, some of the immunosuppressive medications are ones you definitely want to avoid in pregnancy, such as methotrexate, mycophenolate are ones you will want to stop and especially stopping methotrexate a few months before pregnancy, if you can, ideally. And then when it comes to biologic therapy, so there isn't a ton of data about biologic safety for dupilumab, which is the main biologic we use for atopic dermatitis, but from what we've seen so far, there isn't any kind of signals of adverse events.

So, if it's needed, it can be used, but knowing that there really isn't significant evidence out there.

Dr. Mariam Hanna
Okay, so less than a category B medication in this situation, is that right? Okay. Chronic urticaria, another itchy condition.

How do we approach management of chronic spontaneous urticaria during pregnancy, especially when they're having more moderate to severe, more disruptive-type symptoms?

Dr. Lana Rosenfield
So, similar to the other atopic conditions, identify and avoid any triggers or causative factors as best as possible. But then when it comes to medical therapy, mentioned before with treatment of rhinitis, cetirizine, loratadine are going to be your preferred second-generation antihistamines to use, trying to use the lowest dose possible to control symptoms. And then omelizumab does have more reassuring data for humans in pregnancy and has good animal data as well.

So, if patients are having more severe symptoms, omelizumab can be used. And again, similar to atopic dermatitis, there is a lot of mimickers in pregnancy that you want to make sure if symptoms are worsening, it is the chronic spontaneous urticaria and not another pregnancy condition that could be causing similar symptoms.

Dr. Mariam Hanna
Perfect. I like that there are common themes here, going with the least invasive options first and then using your standard oldest therapies that we know have a lot more data on them. And then

if it's not behaving, there are advanced therapies, but there's also make sure you confirm that the diagnosis is still the same diagnosis.

So, definitely some common themes. Okay, I'm excited about food allergies. How do you counsel patients with existing food allergies during pregnancy?

Are there any particular changes in terms of like reaction thresholds that we know about during pregnancy?

Dr. Lana Rosenfield
So, a lot of the ways you counsel your patients is going to be similar in pregnancy and outside of, which is strict avoidance and making sure patients carry their epinephrine autoinjector, as well as rapidly treating symptoms as quick as possible if they do occur, making sure patients have an anaphylactic action plan and that they use it and that they know when to use it. Because we do know that with maternal anaphylaxis, there can be poor fetal outcomes because of the symptoms that do occur. Overall, the clinical manifestations in pregnancy with anaphylaxis aren't that different than you would expect outside of pregnancy.

There can be some different symptoms that do present in pregnancy that you don't see outside of, such as like uterine cramping, lower back pain, because we do know there are mast cells in the uterine wall. So, this can be a factor in patients who are pregnant, but really making sure prompt epi is going to be important for management of a food-related anaphylaxis and making sure patients know to use it because we know that worse outcomes in anaphylaxis come with not using epi early enough and we want to make sure especially patients who are pregnant know that and do use it if they need to.

Dr. Mariam Hanna
So, what I'm hearing is that epinephrine remains the gold standard regardless of pregnant or not and, if anything, prompt recognition and use of epinephrine would still be the best recommendation that we have there.

Dr. Lana Rosenfield
Yes, of course.

Dr. Mariam Hanna
Okay, so let's move on to allergen immunotherapy. There are some patients that will have started allergen immunotherapy before pregnancy. So, let's do those ones first.

Is it safe to continue during pregnancy, subcutaneous or sublingual immunotherapy?

Dr. Lana Rosenfield
So, if patients are already on immunotherapy, it is safe to continue as long as you're not updosing their immunotherapy. So, if they're on buildup, you wouldn't want to increase the dose while they're pregnant. Of course, even if they're on maintenance, it's not without risk.

So, really making sure you have that discussion with the patient about the risk and benefit of the immunotherapy and a patient, even though the risk is low of having a reaction if they're already on maintenance, they might choose to not take that risk and stop. And I think that's not an unreasonable decision if that's what a patient wants to do, but letting them know that it can be continued and that risk is low, but it's not zero. So, continuing immunotherapy if they're already on it, but letting the patient make that decision.

Dr. Mariam Hanna
And the risk specifically when you're discussing it here is anaphylaxis while on treatment or is it due to the allergen itself that they are receiving?

Dr. Lana Rosenfield
So, to the allergen immunotherapy. So, whether it's to the sublingual immunotherapy tablet that they're taking at home or to the injection that's being done at a medical clinic.

Dr. Mariam Hanna
Okay. Is it safe to initiate immunotherapy in a newly diagnosed, let's say, very symptomatic brainitis patient that comes to you that's newly pregnant?

Dr. Lana Rosenfield
No, unfortunately not. So, we would not be offering patients immunotherapy, whether it be sublingual immunotherapy tablets or subcutaneous immunotherapy injections when they are pregnant.

Dr. Mariam Hanna
Okay. We touched a little bit on biologics. They represent largely a new class of medications that we have in the allergy space with some of our older biologics having a little bit more clinical data around them.

What's the current evidence regarding the safety of biologics? What's the current evidence regarding safety of biologics during pregnancy and breastfeeding? Is it a blanket statement on them all or do we have data for separate ones?

Dr. Lana Rosenfield
So, the evidence is quite scarce, but just from basic registry studies specifically for omelizumab, really no evidence of major congenital issues and malformations due to being on the biologic therapy. Again, this will come down to a risk-benefit discussion with the patients that we don't have necessarily a lot of evidence on the safety, but what we've seen is that there isn't evidence of harm from what we know now, but what would be the harm if you were to stop it? So, if a patient's going to have worsening of their asthma and put them at risk for exacerbations, that might be more of a risk than what the medication itself would give.

Really, at this point, we say biologics can be used in pregnancy and breastfeeding, but again, with the understanding that we don't have a large volume of evidence for that safety data, but it's important because it also is a steroid-bearing therapy, so we know that there can be risks with systemic corticosteroids in pregnancy, and then also there's improved quality of life, which also is a factor as well.

Dr. Mariam Hanna
Okay. Can you summarize key go-to references that you use for assessing patient safety or medication safety during pregnancy? There used to be a wonderful website, and we always refer here in Canada to this wonderful website that used to exist that no longer exists.

Are you aware of any other go-to references or resources that you like to use in your practice now?

Dr. Lana Rosenfield
So, if you're looking specifically for pregnancy lactation risks, so there's LactMed and Reprotox are two specific sources for that, but I also have found it quite helpful even looking at specific society guidelines and practice parameters that they are starting to incorporate information on pregnancy and lactation. The product monographs themselves also a lot of time will have the information or even a resource like UpToDate. Any medication that you are interested in, you can go to an information page that would have information on pregnancy and lactation risks.

Dr. Mariam Hanna
Perfect. So, not a one resource for everything, but lots of different resources that are out there depending on the condition and the drug that you are considering. What's your go-to kind of counseling for patients that are hesitant to use the necessary medications to get control of their disease during pregnancy because of fear of their unborn child or fear for the safety of their unborn child?

Dr. Lana Rosenfield
So, as mentioned previously, it is a big discussion about the risk and the benefit of not only being on the medication, but of stopping the medication. So, does the risk of using the medication outweigh the risk of stopping it and having the disease be poorly controlled? No matter what you say, it's still going to be the decision of the patient and you have to be okay with that.

But it's important to make sure that they have all the appropriate information of what is safe, what data is out there, and then they can make that decision if it's something they want to stay on. We can really only guide and we can't make that final decision for the patient.

Dr. Mariam Hanna
Shared decision-making. There you go. That's the plug.

And then adequate follow-up, I guess, in the event that their disease changes and that they need further reconsideration. Okay, so then comes breastfeeding. What should physicians know about managing allergic conditions in the postpartum and breastfeeding period?

Are there major concerns about drug transmission through breast milk for common allergy medications that we use and common being anywhere from antihistamines to nose sprays to the puffers to the topical steroids?

Dr. Lana Rosenfield
So, the most common one we use, antihistamines, there is a minimal amount that does get released in the breast milk. Typically, we would say that's an amount that won't have a significant effect on the baby, but it's not that there isn't. There is a small amount.

I think one thing, though, also to take into account with antihistamines is that there is risks for decreasing milk production. Typically, this wouldn't happen if the patient's breast milk supply has already been established, but especially when a patient is starting to establish that milk supply, it can decrease that milk production. So, if that's an issue, making sure that they're aware of that.

Biologics, again, safety data is quite limited. Really no evidence at this point to indicate a significant risk, but knowing that the data isn't really there. One thing, medication that we do use a lot to take into account is the topical steroids as well.

So, they are considered safe in breastfeeding, trying to use that lowest effective dose, but especially if you're using it in areas where your baby might be touching you to make sure to wash it off before the baby skin's in contact where you've applied the topical steroid, especially if it is in the breast region that they're going to be ingesting as well.

Dr. Mariam Hanna
Yeah.

Dr. Lana Rosenfield
Perfect.

Dr. Mariam Hanna
And in a perfect world, if the allergist was seeing that patient with moderate to severe allergic condition X, is there preconception advice that the allergist could be providing their patient?

Dr. Lana Rosenfield
So, it's important for all these conditions that we try and get them under their best control going into pregnancy, especially something like asthma, where we know having asthma exacerbations and poorly controlled asthma can lead to worse outcomes. So, trying to get therapy to the point where their disease is most controlled. If it's possible, trying to step down to the lowest dose that a patient needs to control that and trying to do that before pregnancy is always going to be ideal.

So, you're not putting any risk of having the disease flaring while pregnant. Like we talked about, there are certain medications that you would potentially want to stop. Methotrexate, JAK inhibitors, topical calcineurin inhibitors that you would want to stop.

So, you would want to have those conversations prior to conception. But again, it's going to be talking with the patient about their preference, knowing the risk and benefits, and knowing that this is something they want to continue throughout pregnancy if they are. And again, patients on immunotherapy, if you are doing that build-up, you may consider stopping the build-up, or a patient may consider stopping that immunotherapy before conceiving.

Dr. Mariam Hanna
Okay. And then, like, finally, and I have a feeling I might know the answer already, but do allergic conditions revert back to pre-pregnancy patterns after delivery?

Dr. Lana Rosenfield
They do, typically. They skew towards normalizing after delivery, yes.

Dr. Mariam Hanna
How should we monitor and support our patients postpartum? We're going to go back to some of their old medications.

Does that sound about right?

Dr. Lana Rosenfield
Yeah. Again, talking about the risk and the benefit of using these medications if they are breastfeeding, because we want to make sure they know if there is any potential risk to the baby. One actually to think about, too, especially in the postpartum period, is going to be Montelukas, because we know about the potential psychiatric side effects, and we know that there can be psychiatric conditions that can happen postpartum as well.

So, wanting to make sure that's something that's monitored probably a little bit more closely than you would previously, but really making sure to support the patient with whatever treatment they're on and making sure that they know what treatment options are there and that they can make that decision of what to be on.

Dr. Mariam Hanna
All right. Time to wrap up and ask today's allergist, Dr. Lana Rosenfield, for her top three key messages to impart to patients and physicians on today's topic, allergic conditions in pregnancy. Dr. Rosenfield, over to you.

Dr. Lana Rosenfield

Okay. So, the first thing I would think is key is to try and get the patient to the lowest effective dose to help manage their disease. So, we know a lot of these medications are safe, but are they 100% safe?

A lot of times we can't say for sure, so really try to get them to the lowest dose that helps control their disease and their symptoms. The second thing I would say is don't forget about the non-pharmacologic therapies. So, using the nasal saline, avoiding triggers are going to be things that you want to emphasize further when we're talking in pregnancy because we do want to make sure that patients have the best control, but also have the best control with the lowest medications possible.

And then for number three, I think, like we talked about throughout this whole talk today, is having a shared discussion with the patients, discussing the risk and benefits with whatever treatment option you are considering. If you don't know what the risks are of the medications, going to those resources, looking it up, and really supporting the decision of the patient that they make.

Dr. Mariam Hanna
Thank you, Dr. Rosenfield, for joining us on today's episode of The Allergist.

Dr. Lana Rosenfield
Thank you so much for having me.

This podcast is brought to you by the Canadian Society of Allergy and Clinical Immunology and produced in collaboration with PodCraft Productions.