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My name is Mehret Birru Talabi. I'm an Assistant Professor of Medicine in the Division of Rheumatology and Clinical Immunology. Thank you for the opportunity to speak with you today about reproductive health in women with systemic autoimmune disease. I have no disclosures.

So we'll first discuss some basic principles around immunity and hormones. Our talk today is going to focus on lupus and antiphospholipid antibodies, and we'll discuss two relevant clinical cases related to these disease entities-- pregnancy and contraception management.

So at a high level, let me first address how sex hormones might affect the immune system. Sex hormones, including estrogens and progesterone, help to regulate the innate and adaptive immune systems through multiple pathways and by means of receptors on immune cells. Estrogens act via two estrogen receptors-- estrogen receptor alpha and estrogen receptor beta-- and they're widely distributed on T cells, B cells, macrophages, and dendritic cells.

Estrogen receptor alpha has been associated with the production of type 1 interferons, whereas estrogen receptor beta is more anti-inflammatory and may be expressed less in T cells. Progesterone appears to be more anti-inflammatory as a whole, and it tends to facilitate the differentiation of T helper cells into T regulatory cells, which may actually be protective against autoimmunity.

So high estrogen states, and perhaps through the actions of estrogen receptor alpha specifically, may be more pro-inflammatory than progesterone. I'm going to use pregnancy as a high estrogen state in this example. So Th1-type and Th17-type cells and cytokines have been identified as major causes of allograft rejection in transplant settings. And if you conceptualize pregnancy as being a transplanted organ, as not all of the fetal DNA is maternal, you can imagine that a pregnant person's immune system has to adjust so that it doesn't reject or destroy a developing fetus.

And one of the ways it seems to do so is by shifting away from Th1 and Th17 cells in cytokines and towards Th2 cells and cytokines, generally promoting fetal tolerance and helping to ensure pregnancy success. One problem is that autoimmune disease, the disease that we as rheumatologists help to treat, often involve disordered populations of either Th1 or Th2 or Th17-type cells. So if you shift the immune system through high estrogen states, like pregnancy, away from Th1, then diseases that involve disordered Th1 cells and cytokines tend to get better.

And that might be why rheumatoid arthritis, one of the prototypic diseases that we treat in rheumatology, tends to get better during pregnancy. And conversely, diseases such as systemic lupus erythematosus are caused by abnormal and disordered populations of Th2 cells and cytokines. And if you shift the immune system to favor this disturbed and dysfunctional system, you might get potentiation of disease activity.

And this may be one reason that lupus tends to worsen during pregnancy. And we might see a similar effect on disease activity actually with exposure to high concentrations of synthetic estrogens, perhaps the old oral contraceptives that had a lot of estradiol or hormone replacement therapy for assisted reproductive technologies.

So I think an important point is that some autoimmune diseases tend to worsen during pregnancy and some tend to get better. Not for everybody, but trend towards getting better during pregnancy. And one of the reasons might be because of differential effects of the high estrogen state of pregnancy on the immune systems of people who have dysfunctional immune systems at baseline.

So people with rheumatic diseases can die from pregnancy, and that's why pregnancy is such an important disease state to think about among these patients. Rheumatic disease as a term encompasses people with autoimmune and connective tissue disorders that again we as rheumatologists treat. When we think about diseases that worsen in the context of pregnancy in rheumatology, we will often think about uncontrolled systemic lupus erythematosus, which I just mentioned to you, and antiphospholipid syndrome, which is a clotting problem that's autoimmune mediated and occurs among 25% to up to 40% of patients who also have lupus.

These two conditions are associated with the highest risk of maternal mortality that we probably deal with in the rheumatology world, up to 5 to 20 times higher than that of the general population as described by Dr. Megan Clowse and Dr. Bella Mehta more recently. Today we're going to spend the most time talking about lupus and people who have antiphospholipid antibodies.

But I do want to mention that maternal and neonatal outcomes are potentially adverse in many other rheumatic diseases, including Sjögren's syndrome, vasculitis, scleroderma or systemic sclerosis, myositis, spondyloarthritis, including psoriatic arthritis, and yes, even rheumatoid arthritis, which I just told you tends to improve during pregnancy. We know that roughly about a third of patients will have disease activity throughout their pregnancies.

And what happens? We can see complications such as miscarriage, stillbirth, preterm birth, growth restriction, and preeclampsia that affect these pregnancies. The high estrogen state of pregnancy can also potentiate thrombotic events, which also can lead to adverse outcomes, particularly among people who at baseline have an increased risk of thrombosis due to their disease state, and that might be our antiphospholipid syndrome patients.

Generally, as a principle, some people are going to do very well during pregnancy if they have a rheumatic disease. And what we understand is that by controlling disease activity, for approximately three to six months prior to pregnancy, pregnant people will have a significantly better chance at experiencing a healthy pregnancy. So controlled disease activity, people enter pregnancy with their diseases well controlled, and they tend to do better. And that's why pre-pregnancy counseling is so important for people with rheumatic diseases, including those with the diseases that we worry about the most in rheumatology.

So I've alluded to these disease states. I want to mention them in greater detail in the following slides. The first disease state is systemic lupus erythematosus, SLE. This is an autoimmune disease that results in inflammation and tissue damage, and this is a disease primarily of females and people born female. In general, I'll mention patients with autoimmune diseases tend to be female. In rheumatology, that means about 80% or so of our patients are female, so we are indeed a women's health specialty.

Now, back to lupus. The prevalence of lupus peaks in reproductive years, underscoring the importance of discussing lupus with you today with respect to reproductive health. It also disproportionately affects females of color, including Indigenous and Native peoples, Black Americans, Latinx, and Asian people. The disease is characterized by flares and spontaneous remission. And importantly, this disease can affect just about any organ, including classically the skin, and this is an example of the malar or butterfly rash It can also affect the joints, cardiovascular system, kidneys, and nervous system, lungs.

Antiphospholipid antibodies are not a disease state by themselves, but if accompanied by clinical clotting or vascular events can be categorized as the antiphospholipid syndrome which will necessitate anticoagulation. Antiphospholipid antibodies can attack and damage proteins that bind the phospholipids of the walls of blood cells. And the antibodies we're talking about include the lupus anticoagulant, beta 2 glycoprotein antibody, and anticardiolipin antibody.

Lupus anticoagulant is somewhat of a misnomer, because even though the word "anticoagulant" is in the term, it actually increases the risk of thrombosis by about 4 to 16-fold. Of the antiphospholipid antibodies, it's probably associated with the greatest risk of thrombosis. There is also a varying association between thrombosis and beta 2 glycoprotein antibodies and anticardiolipin antibodies, but generally, the higher the titer, the greater the risk of a thrombotic event. And the risk might be the highest among people who have all of these-- LAC, beta 2 glycoprotein, and anticardiolipin antibodies.

I've mentioned antiphospholipid syndrome, which is the presence of antiphospholipid antibodies and evidence of microvascular, macrovascular, obstetric, hematologic, and cardiac valvular clinical issues. I just want to share this reference with you. It's the brand new American College of Rheumatology, ACR, European League Against Rheumatism, EULAR, Classification Criteria for Antiphospholipid Syndrome. And that's probably going to refine the way that we classify people as having APS moving forward, at least in the rheumatology context.

So I would encourage you to review these criteria independently, relevant to your practice. APS Management is going to be out of the realm of this talk. Usually, we will involve our hematology colleagues to help us to manage patients who have APS.

And then, finally here, let me introduce another set of guidelines to you. These are the inaugural American College of Rheumatology Reproductive Health Guideline, which we also call the RHG, and this provides clinicians with a comprehensive framework for the reproductive health care and management of patients with rheumatic diseases. This is not just for rheumatologists. Any of you who are co-managing a patient with a rheumatic disease, these guidelines are also for you.

I was honored to serve on the guidelines committee, and we published this reference in 2020. We're starting to work on the updated recommendations now. There are QR codes here for you to avail to access the manuscript, and all of my management recommendations today will come from the evidence-based recommendations of the RHG.

All right. So as I mentioned, systemic lupus erythematosus, it's a disease that can worsen with pregnancy. Let's talk through a case of a person with lupus who is planning for pregnancy. This is Michelle. She's 25. She has lupus diagnosed at age 21 with disease manifestations of photosensitive rash, oral ulcers, recurrent pericarditis, and inflammatory arthritis.

Serologic profile is a high titer antinuclear antibody and a speckled pattern, more specific for autoimmune disease. She was referred to the UPMC Women's and Reproductive Health Rheumatology Clinic, which I direct at Magee-Womens Hospital, to have a conversation about pregnancy planning. And this is one of the consultation services that my clinic at Magee does provide for patients with rheumatic diseases.

We have a wonderful cadre of subspecialty providers that we work with. Rheumatologists in the network, OB/GYNs and maternal fetal medicine experts may all refer patients to me for pre-pregnancy counseling or pregnancy management. So at Michelle's initial visit with me, she said she's feeling pretty well. Some fatigue occasionally but generally OK. Hasn't had a flare in a while.

Her exam is normal, but her recent labs demonstrated that she's got low complements and double-stranded DNA, so suggestive of some immune activation and maybe subclinical disease activity. She's prescribed hydroxychloroquine, which is the cornerstone of lupus treatment, as well as methotrexate, which has efficacy in treating the rashes and inflammatory arthritis. Among other disease manifestations of lupus, we use this medication widely in rheumatology.

I want to indicate here that methotrexate is a teratogen. We're going to get back to this concept in a minute. Michelle says that she's not experienced pregnancy. She wants to conceive in the next couple of months. And as a reproductive rheumatologist, what are the things that I need to talk with her about to help to prepare her for pregnancy and help her to manage her care if and when she does become pregnant?

All right. So as I mentioned, people with lupus can have more complicated pregnancies. Maternal flares are pretty common, 25% to 60%. And as I alluded to before, people who go into disease with active disease are more likely to flare, and these flares can be life-threatening. Preeclampsia risk is at least two-fold higher among patients with lupus than healthy patients, and the risk is even higher if they also have antiphospholipid antibodies. As I mentioned, a number of our patients with lupus have antiphospholipid antibodies or the actual syndrome.

There are a number of fetal complications that are related to placental dysfunction, including growth restriction, preterm delivery, and fetal loss that I alluded to earlier. I just want to mention preeclampsia. Preeclampsia prevention and management is probably going to change somewhat in the US in the coming years. I just want to mention this entity to you because it's one of the top causes of US maternal death, and it complicates the pregnancies of many of our patients.

This is a condition that occurs in the later stages of pregnancy, greater than 20 weeks of gestation. It's marked by toxic hypertension, essentially, and it appears to relate to placental insufficiency. Maybe that's caused by clotting throughout the placental vasculature due to antiphospholipid antibodies, perhaps due to a pro-inflammatory state.

Treatment is delivery of the fetus. Again, this is a condition that arises quite commonly in rheumatic disease pregnancy. It can develop into multi-organ failure, and we're going to discuss prevention in a few slides.

So we talked about some of the potential complications that arise in lupus pregnancy. But as I framed this, some patients can actually have safe and healthy pregnancies, including lupus patients. So how do we avoid the adverse pregnancy outcomes, and how do we get to the good outcomes?

So when a patient like Michelle comes to see us in clinic, and she's not already pregnant, we have a really important opportunity to try to medically optimize her in advance of pregnancy again to minimize the adverse outcomes that I was telling you about. Michelle has my attention because even though she's feeling OK, her lab suggests that her disease might be a bit active.

So the American College of Rheumatology Reproductive Health Guideline that I introduced you to previously has specific recommendations for our patients with lupus. So here we see that patients should continue hydroxychloroquine if they're using it. Michelle is using hydroxychloroquine. Again, wonder drug in lupus.

If she's not on it for some reason, and doesn't have a contraindication to it, we'd start it or restart it potentially in the context of pregnancy planning. We would need to consider starting a low-dose aspirin towards the end of the first trimester. That's for preeclampsia prevention, and I'm going to circle back to this. And then, we'd want to do a laboratory assessment of her disease activity at least once per trimester.

Let's talk some more about these recommendations. So medications are really important to discuss with patients in the rheumatology context because some of our most effective medications are not compatible with pregnancy, but we do have options. So hydroxychloroquine, I mentioned. This is being a cornerstone treatment for lupus. It's safe and compatible with both pregnancy and breastfeeding.

It reduces lupus disease activity. It reduces the risk of preeclampsia in some studies and preterm birth. And so, again, hydroxychloroquine, well studied, generally great outcomes. That's a medication we would want Michelle to continue.

Michelle was also prescribed to methotrexate. As indicated, that is a teratogen. It's associated with an increased risk, about 40%, pregnancy loss as well as congenital anomalies. So in the next slides, let's talk a little bit more about medication safety and how we're going to think about adjusting Michelle's medications in advance of pregnancy.

The following slides come from table 3 in the Reproductive Health Guideline, and they present the safety of various meds that we use in the rheumatology context prior to pregnancy, during pregnancy, and during breastfeeding. So blue is generally safe to use. And you'll notice that not just hydroxychloroquine but other medications are safe to use during pregnancy, including sulfasalazine, colchicine, azathioprine, prednisone at doses less than 20 milligrams a day. That's the point at which the prednisone is probably not crossing into the fetal circulation. And then, cyclosporin and tacrolimus.

Traditionally, I'll note that steroids have probably been overused during lupus pregnancy. That might be avoidable because we do have options, like azathioprine and tacrolimus and cyclosporin that we can use, and can help us to avoid needing to give high-dose steroids. And we've seen in some cohorts of people with rheumatic diseases that pregnancies exposed to high-dose steroids are associated with preterm birth, small for gestational age neonates, low birth weight, adrenal insufficiency in the neonate, NICU hospitalizations, maternal diabetes, adrenal insufficiency in the pregnant person, hypertension in the pregnant person.

So for Michelle, it looks like she has a little bit of disease activity. I can either monitor her on hydroxychloroquine alone or think about switching her to one of these safer medications, probably azathioprine. She doesn't have renal disease, so probably not tacrolimus. And I want to watch her for three to six months, see if her disease remains relatively quiet prior to pregnancy, if that's compatible with her wishes as well.

Some of the medications that I'm going to present here are not necessarily ones we would use for Michelle for lupus, but I want to mention them to you because they're widely used across other rheumatic diseases, and these are biologic medications, and some have demonstrated safety during pregnancy. These big, bulky molecules are difficult to transport across the placenta during the time at which fetal organogenesis is occurring, so these medications generally are not thought to cause congenital anomalies.

The bigger issue is that they do cross the placenta at later stages of pregnancy and can immunosuppress the fetus, and naturally the neonate could be not only immune suppressed but have circulating drug in their system at the time of delivery. These medications here are called TNF alpha inhibitors. We use them a lot in rheumatoid arthritis, spondyloarthritis, in general, and we don't worry about the TNF alpha inhibitors until the later stages of pregnancy. These are compatible with pregnancy and breastfeeding.

But in the Reproductive Health Guideline, we recommend that if a patient's disease activity is quiet around the third trimester, consider discontinuing the medication a few half lives before delivery, and that's really just because of the concern of immunosuppression in the neonate. I will mention that across multiple studies, children born with TNF alpha exposure do not have an increased risk of serious infections, so we will continue these medications if needed to control maternal disease activity.

Rituximab, we use that in a number of different contexts within and outside of rheumatology. It looks to be fairly safe during pregnancy. At later stages of pregnancy, it can be associated with B cell depletion in the fetus, ultimately the neonate. So most rheumatologists, at least, would want to give the final dose of rituximab during pregnancy some time in the first trimester, very early in the second trimester.

We do have limited safety data for a number of our other biologics. But again, because of their molecular properties and size, they are probably not going to cause congenital anomalies. And again, these medications generally seem to be OK, safe to use during breastfeeding.

So I told you what's safe. Let me tell you what is not compatible with pregnancy. I've already mentioned methotrexate to you, which Michelle was using. Leflunomide, mycophenolate mofetil and its cousin mycophenolic acid, we use that a lot in lupus. Cyclophosphamide, thalidomide, both of which we use in lupus. These are not medications that are compatible with pregnancy and are associated with congenital anomalies.

If we do have somebody who's got life and organ-threatening disease in the second or third trimester, we might consider giving cyclophosphamide in that case, but otherwise, I would say most rheumatologists would try to avoid these medications during pregnancy and during breastfeeding. Some of you may have heard about the small molecule medications we're using increasingly for inflammatory arthritis or even eczema, and these are likely able to cross the placenta and into the breast milk, so at this point shouldn't be used in either the pregnancy or lactation time frames.

So we talked about transitioning Michelle from pregnancy incompatible medications to pregnancy compatible medications in advance of pregnancy. And let's say she does become pregnant. What is going to be the management plan during pregnancy?

And labs are really important to track because the trend gives us a lot of information. As I showed you, our guidelines suggest checking at least once a trimester. I will certainly check more often, if needed, if somebody has active disease. Well, why should we trend the labs? Because the changes of normal pregnancy can be difficult on their own to differentiate from lupus flares, again, using just the blood work.

Complements, C3 and C4, those are the ones we routinely order in rheumatology, they tend to be low when the immune system is activated, will naturally increase during a normal pregnancy, including among patients with lupus. This could mask a flare. Physiologic proteinuria, really common below a level of 300 milligrams a day in pregnancy, but a little protein in a patient who's not pregnant with lupus might concern us for developing lupus nephritis.

The erythrocyte sedimentation rate and inflammatory marker naturally increases during pregnancy. It's a lot less useful to us to check as it doesn't correlate well with active disease during pregnancy. CRP is actually more useful. And then, mild anemia and thrombocytopenia are common in pregnancy. But when we start seeing drops of 30% to 50% with the platelets, and certainly going down below 100,000, we start getting worried for lupus flare. So for Michelle, if and when she becomes pregnant, we'd optimally see her in clinic, check her physical exam, and we would generally plan on checking her labs periodically during the pregnancy.

I've mentioned preeclampsia to you already and also our RHG recommendation to start low-dose aspirin among patients who have systemic lupus erythematosus or antiphospholipid antibodies or syndrome. Why? Again, preeclampsia affects a number of the pregnancies that occur in lupus and antiphospholipid syndrome.

So to reduce the risk of preeclampsia by only about 10% to 15% actually, the American College of Obstetricians and Gynecologists and the US Preventive Health Task Force have recommended that low-dose aspirin is initiated between 12 and 28 weeks of gestation and continued daily until delivery. I want to mention that we're focusing on lupus here, but we also know that patients with rheumatoid arthritis, psoriatic arthritis, and vasculitis have about a two-fold or higher risk of preeclampsia as well. So I think, over time, we're going to see that our recommendations are liberalized, and more patients with chronic medical conditions in general are going to be added to these recommendations.

So for Michelle, someone with lupus who does not have antiphospholipid antibodies, I'd start low-dose aspirin. If she did have antiphospholipid antibodies or antiphospholipid syndrome, I would start low-dose aspirin all around the end of the first trimester. And our phenomenal maternal fetal medicine and OB/GYN colleagues have usually done that for our patients as well.

We've talked about a number of issues related to lupus pregnancy, pre-pregnancy counseling, and pregnancy management. The important thing to think about is that we really need to talk about reproductive planning, if at all possible, with patients with lupus to try to get the medications and diseases under control to facilitate healthy pregnancies.

We need to consider the use of hydroxychloroquine in all patients who have lupus. We need to review other medications for safety. We need to track labs. And we need to consider low-dose aspirin, Guideline's concordant recommendation here, at around 12 weeks of gestation to reduce the risk of preeclampsia.

All right. So next, we're going to briefly talk about contraception in the patient with autoimmunity. And this is Maya. She has a long-standing history of lupus. At this point, she's doing fairly well, but her serologic profile does reveal that she has a lupus anticoagulant.

She's using hydroxychloroquine. Again, our cornerstone medication for lupus. But she's also using mycophenolate, which is a teratogen medication. She does have a history of preeclampsia in a prior pregnancy, and she really wants to avoid pregnancy moving forward, but she is using condoms. She wants to consider her other options. What's safe and effective to use in the context of her disease?

I'll just mention that the fact that she's using a teratogenic medication, that she doesn't want a future pregnancy that would be undesired, and getting pregnant would be a difficult situation, the condoms would not be ideal in this situation. They are a behavioral method of birth control that requires the cooperation of another person, so let's talk a little bit about what methods might be more effective and safe for Maya.

So we're going to talk about effectiveness first. This is not always the thing that is most important to patients, but I will mention this to frame our conversation today. People also talk about side effects, et cetera, which is going to be outside of the scope of today's talk. We do have highly effective methods of contraception, including the subdermal implant, the intrauterine device or IUD, and surgical sterilization.

The implant is actually more effective than sterilization, and it is a reversible method of birth control. So implant, intrauterine device, they last for years and they're reversible. Low risk of failure with these methods.

Any method that's going to require somebody to remember to take it periodically is not going to be as effective in the real world. So we do have options here. We have the estrogen-containing patch; the mini pill, which is progestin only; the estrogen-containing vaginal ring; the combination pill of estrogen and progestin; and the Depo shot, which is progestin only.

Least effective of our options are the barrier methods and fertility awareness, spermicide. And people who use these methods generally don't want to be pregnant, but these are fairly inadequate at preventing pregnancy. But they're great options for birth control compared with the more effective method of contraception.

So what are Maya's options for birth control that might be safe, given the fact that she has lupus and she has a predisposition towards clotting due to the lack of positivity? And remember, as we talked about, exogenous estrogens could precipitate disease activity in lupus. So we know that there are some risks associated with estrogens and lupus, so let's talk through this a little bit.

First, estrogen increases the risk of thrombosis among all people, and estrogen-containing contraception is associated with a 2 to 5-fold higher risk of venous thromboembolism, stroke, or myocardial infarction in the general population. They do not have commensurate data for patients with rheumatic diseases, but the absolute risk of a thrombotic event is actually fairly low. As mentioned, we don't have a lot of data about contraception safety in patients who have antiphospholipid antibodies or APS, but it's generally thought that the risk of thrombosis with estrogens is unacceptably high for people with antiphospholipid antibodies, and we should avoid them.

What if Maya didn't have lupus anticoagulant and just had lupus? Could she use estrogen safely? Well, there are actually two well-done randomized controlled trials that answer this question, and both were very consistent in suggesting that estrogen-containing contraception is safe and stable in lupus. These studies did not focus on patients with active lupus or highly active lupus, but for our stable patients, they can use estrogen-containing contraception safely.

So let's get back to the Reproductive Health Guideline. I want to mention here that we are very clear in the guideline that every patient with a rheumatic disease can use a safe and effective method of contraception. And here, we're going to focus on reversible methods of contraception, not sterilization. So if we have someone like Maya, she would be in this set of boxes here as having a positive antiphospholipid antibody, and IUDs or progestin-only pill would be considered safe methods of contraception for Maya.

If she didn't but she had lupus disease activity, one thing to note, if you go back and look at this slide or the guideline is that estrogens, again, can be used. If the disease activity is moderate to high, progestin-only would be preferred. And people who are not lupus patients and don't have antiphospholipid antibodies can use just about any method of contraception from a safety perspective.

Just to put this in a little bit more of a clear presentation for you, these methods appear to be safe for all of our patients, including those who have lupus and antiphospholipid antibodies-- the implant; progestin-only; the intrauterine device, which is either non-hormonal or progestin-only; and the mini pill, which is progestin-only. I'll mention the progestin-only pill will be available as an over-the-counter medication in early 2024. And again, this medication is safe for patients like Maya.

We don't know what the cost is going to be, but for somebody who has lupus and antiphospholipid antibodies, this might be a medication that's more efficacious than using barrier methods of contraception and presumably will not increase her disease activity. What else is available? Emergency contraception. Not effective long-term for contraception, but this is progestin-only.

These methods are not abortifacients, and in fact, the FDA has determined as of December 2022 that they are not abortifacient, and that's described in a recent JAMA viewpoint. These medications are effective for several days after unprotected sex. The effectiveness wanes with each successive day.

And some pills are over-the-counter. I tend to prescribe these to patients with the hope that their insurance will cover some of the cost. And I recommend that if they're going to have it, they just put it in the sock drawer or put it away somewhere, to use it when they need to.

So some take-home points. We've got Maya who's got lupus, and she has antiphospholipid antibodies. First, I want to emphasize that every patient with rheumatic diseases can use at least one contraceptive method safely.

I think it's just important to mention this point again because we've looked at data for patients with rheumatic diseases in the UPMC system, and what we found is actually what we have found in other studies nationwide, which is only about a third of patients with rheumatic diseases are prescribed contraception, moderately effective or highly effective, even though they have diseases that can worsen in the context of pregnancy, even though many of our patients are prescribed teratogenic medications for disease control. And that appears to be a lower utilization of contraception than what is seen in the general population of people.

So hormones can be safe to use in patients, even those patients who have lupus. We do have to be careful about exogenous estrogens among patients who have antiphospholipid antibodies. And one exception I'll mention with lupus is the estrogen patch. The estrogen patch, and we explicitly mention this in the Reproductive Health Guidelines schematic, seems to have higher levels of exogenous estrogen, and we're not sure about its safety profile yet in patients with rheumatic diseases. We would hold on that for now.

Finally, when we think about the methods that any provider can prescribe, including those who do not have the ability or the skill set to insert an IUD or a subdermal implant, the progestin-only mini pill. That can be used for patients. The emergency contraceptive method can also be used, although not a great long-term option.

I hope some of this talk was helpful or at least informative for how we might conceptualize the care of a patient or patients with rheumatic diseases, particularly those that can worsen during pregnancy and are complicated by other factors, such as thrombogenicity and teratogenic medication use. It's been a pleasure to be with you today.

Thank you for your time, and want to encourage you, if you have a patient with rheumatic diseases who's contemplating pregnancy or has a contraceptive need or is considering fertility treatments, send me a referral via email. I'd be happy to work with you and contribute to the care of that patient. We also have e-consults available if you look under Reproductive, Women's Health and Med Safety.

Thank you for all of the support that has certainly been given for my awards, colleagues, and multidisciplinary colleagues across this institution, and most importantly, the patients who certainly have taught me so much and have introduced me into their lives. Thank you.