RHEUMATOLOGY NURSE
PRACTICE

Inside this Issue

ISSUE 7 | VOLUME 3

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FAMILY PLANNING & PREGNANCY ISSUES IN RA

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TARGET AUDIENCE

This activity has been designed to meet the educational needs of nurses and nurse practitioners. Other healthcare providers may also participate.

ACTIVITY DESCRIPTION

In this issue of *Rheumatology Nurse Practice*, we will explore emerging standards for the care of pregnant women with RA, including the role of new drug labeling rules and pregnancy registries in developing a better understanding of pregnancy-related drug safety. We will also explore considerations for women who are breastfeeding as well as for male patients with RA who are making family planning decisions.

LEARNING OBJECTIVES

After participating in the activity, learners should be better able to:

- Assess the expanded role of rheumatology providers in providing drug-appropriate information to patients who are pregnant or trying to get pregnant in light of the new Pregnancy and Lactation Labeling Rule
- Analyze results from key registry studies that have explored possible predictors of clinical status among patients with RA during and following pregnancy
- Discuss appropriate guidance that should be offered to both women and men with RA making family planning decisions
- Develop a checklist of key information to suggest to new parents with RA that with help ease their transition into parenthood while keeping their disease under control

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This newsletter was reviewed by **Carrie Beach, RN, BSN**. Ms. Beach has disclosed the following relationships: Pfizer, Horizon, Novartis/A.

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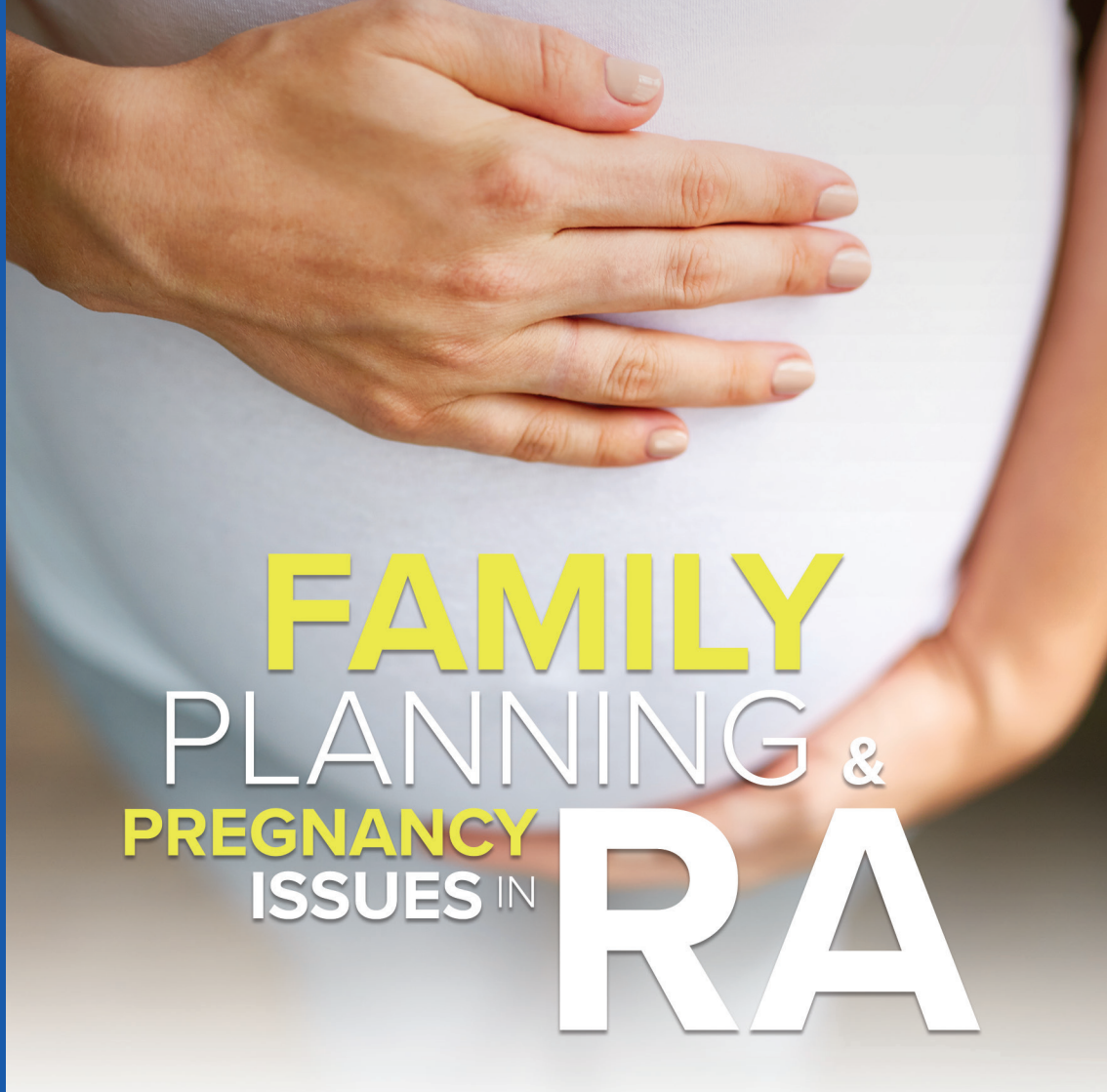

FAMILY PLANNING & PREGNANCY ISSUES IN RA

Rheumatoid arthritis (RA) affects many women and men in their reproductive years, when family planning decisions may influence choices around disease management. Achieving low disease activity prior to conception is critical for minimizing the risk of adverse pregnancy outcomes. The selection of therapy during pregnancy and the post-pregnancy breastfeeding period requires a delicate balance between maintaining disease control and limiting the potential for toxicity to the fetus and newborn. Each step of the family planning process requires open communication between patients with RA and their rheumatology providers.

Clear guidance on pregnancy-related treatment decisions in RA is limited. Much of what is known about the safety of synthetic disease-modifying antirheumatic drugs (DMARDs) and biologics in RA is extrapolated from research in other immune-mediated diseases, notably Crohn's disease, inflammatory bowel disease (IBD), and systemic lupus erythematosus (SLE). A review of the latest evidence in pregnancy-related RA management is necessary to counsel women and men with RA who are planning to start a family.

ACCREDITATION AND CREDIT DESIGNATION

Nurses

Rheumatology Nurses Society is accredited as a provider of continuing nursing education by the American Nurses Credentialing Center's Commission on Accreditation.

Rheumatology Nurses Society designates this educational activity for 3.42 total contact hours and 1.15 CNE pharmacotherapeutic contact hours.

METHOD OF PARTICIPATION

There are no fees to participate in the activity. Participants must review the activity information including the learning objectives and disclosure statements, as well as the content of the activity. To receive CNE credit for your participation, please go to **rnsnurse.com/rnpce** and complete the post-test (achieving a passing grade of 70% or greater) and program evaluation. Your certificate will be emailed to you upon completion.

Drug Names Included Within This Issue

GENERIC	BRAND
Adalimumab	Humira
Etanercept	Enbrel
Abatacept	Orencia
Certolizumab pegol	Cimzia
Tocilizumab	Actemra
Tofacitinib	Xeljanz
Ustekinumab	Stelara
Teriflunomide	Aubagio
Apremilast	Otezla
Alefacept	Amevive
Golimumab	Simponi
Infliximab	Remicade
Natalizumab	Tysabri
Rituximab	Rituxan
Sarilumab	Kevzara

Understanding Medication Safety: Pregnancy Ratings and Drug Labels

The U.S. Food and Drug Administration (FDA) system for presenting pregnancy-related medication safety information is evolving. The former letter-based rating system and new drug labeling rules were designed to support providers involved in preconception counseling and pregnancy-related treatment decisions.

ABCDX Ratings

After the thalidomide disaster in the 1960s, clinicians were presented with an increasing amount of pregnancy-related safety data from human and animal studies that varied in quality.[1] In 1979, the FDA introduced the letter-based rating system in an attempt to standardize the presentation of pregnancy-related medication safety data.[1] The five categories (A, B, C, D, and X) indicated a different risk-benefit ratio based on available information in animal and human studies (Table 1).

Although the ABCDX system achieved the goal of providing a framework for discussing medication safety, the categories were deemed to have many limitations.[1] For example, **Category A** is reserved for medications with the highest-quality controlled clinical trials in pregnant women showing no risk to the fetus. This is a high bar to reach, and only 0.7% of drugs approved in the United States are therefore classified as Category A.[1]

New medications are more easily allocated to **Category B**, which requires animal studies showing a lack of harm but does not require any evidence in humans.[1] Medications can remain in Category B as long as they remain untested in pregnant women. Therefore, the only way to identify risk from Category B medications to pregnant women or fetuses may be through voluntary adverse event reporting or pregnancy registries after these drugs are approved and widely prescribed.

The majority of medications in the United States are allocated to **Category C**, which indicates that the potential for harm cannot be excluded.[1] Medications can be classified as Category C when animal studies suggest a potential for fetal harm, and no human evidence is available to refute that observation. Many older and established medications are labeled Category C despite decades of use in pregnant women with few reports of adverse effects simply because they were never tested in controlled human trials. On a practical level, the Category C classification often translates to "we don't know," which is not helpful for patient counseling or treatment decision making.[1]

Downfall of the Letter Rating System

As experience with the ABCDX system grew, experts began to argue that the categories were more than just limited—they were misleading. The "innocent until proven guilty" approach to evidence meant that untested drugs without known side effects (Category B) were regarded as safer than tested drugs with known side effects (Category C). To balance this contradiction, clinicians were advised to use caution when considering newer medications labeled Category B, while continuing to use Category C medications based on their long track records of safety. Category D medications also remained appropriate in specific clinical circumstances and could be used with minimal risk under close supervision.[1]

Frustration with the labeling system culminated in 1997, when the FDA held a public hearing to discuss options for revising the ABCDX categories.[2] Based on feedback from the FDA hearing and input from the Teratology Society, the healthcare community identified 5 major limitations of the pregnancy category system:[2]

1. The categories are overly simplistic and do not effectively communicate risk
2. The categories wrongly give the impression that risk increases steadily from A to X, and that drugs within the same category carry the same potential for risk

Table 1 *Pregnancy Categories Prior to the New Labeling Rule*[1,16,27]

CATEGORY	RISK	EXAMPLES
A	Controlled clinical studies in humans have failed to demonstrate a risk to the fetus in the first trimester of pregnancy, and no evidence exists suggesting risk in later trimesters.	• Folic acid
B	Reproduction studies in animals have failed to demonstrate evidence of impaired fertility or harm to the fetus. However, no controlled clinical studies have been conducted in humans.	• Anakinra • TNF inhibitors
C	Reproduction studies in animals have either not been performed or have demonstrated evidence of impaired fertility or harm to the fetus. However, the benefit of the drug may still outweigh its risk.	• Hydroxychloroquine • Sulfasalazine • Non-TNF biologics
D	Adverse reaction data in human investigational trials or marketing experience has been demonstrated. However, the benefit of the drug may still outweigh its risk, especially in emergency presentations.	• Azathioprine • Cyclophosphamide
X	Studies in animals or humans have demonstrated fetal abnormalities or there is positive evidence of fetal risk based on adverse reaction reports from investigational or marketing experience, or both. The risk of using the drug clearly outweighs any possible benefit.	• Leflunomide • Methotrexate

3. The categories do not differentiate between evidence from animal and human studies
4. The categories do not discriminate between potential adverse effects, conveying no information about the type of harm, incidence, or severity, or the role of drug dose, duration, frequency or route of administration, or timing of gestational exposure
5. The categories describe planned prescribing only and do not address risk associated with unintended drug exposure

The Pregnancy and Lactation Labeling Rule

Rather than tweak the rating system, the FDA discontinued the ABCDX pregnancy risk categories altogether. In December 2014, the FDA passed the Pregnancy and Lactation Labeling Rule (PLLR) to establish new drug labeling requirements, effectively ushering in a new system for discussing pregnancy-related medication safety.

Under the PLLR system, all prescription medication labels must include narrative text that describes the safety information for the drug. To address concerns from the ABCDX era, such as the lack of differentiation between human and animal data, the narrative text must be organized and presented according to several guiding principles (Table 2). Relevant narrative text appears in Section 8 of all drug labels and includes information in 3 subsections:

- Section 8.1: Pregnancy
- Section 8.2: Lactation
- Section 8.3: Female and male patients of reproductive potential

The PLLR took effect on June 30, 2015. All new medications approved since June 30, 2015, are required to comply with the new labeling rule and will not be issued an ABCDX category. Labels for medications approved before June 30, 2015, are required to be updated on a phased schedule based on their original approval date. Manufacturers have been given 3–5 years to meet the new labeling requirements, meaning that many labels will not be PLLR-compliant until 2018 to 2020. During the transition from ABCDX to PLLR, healthcare professionals must consider safety information from both rating systems as they counsel their patients who are pregnant or may soon become pregnant.

The PLLR in Real-World Practice

As the PLLR system is relatively new, it may be too early to tell how well it is being received by the medical community. Compared with ABCDX categories, the PLLR system shifts more responsibility onto healthcare professionals to read lengthy product information and

Table 2 *Pregnancy and Lactation Labeling Rule (PLLR) Requirements*[1,38]

LABEL SUBSECTION	DETAILS
Pregnancy Registry	• If a pregnancy registry is available, this section must contain a statement about the registry and registry contact information

Risk Summary	• When the drug is contraindicated, this must be stated first
	• Risk statements must be presented in the following order: based on human data, based on animal data, based on pharmacologic studies
	• When **human data** are available, the risk summary must include:
	  ▪ Specific development outcome
	  ▪ Incidence of developmental outcome
	  ▪ Effects of dose, duration, and gestational timing of exposure
	• When **animal data** are available, the risk summary must include information about the species affected, timing, dose, and outcomes, and summarize these findings to describe the potential risk for adverse developmental outcomes in humans
	• When the drug has a mechanism of action (MOA) known to result in adverse developmental outcomes, the risk summary must explain the MOA and potential risks

Clinical Considerations	• This section summarizes relevant information under several headings:
	  ▪ Disease-associated maternal and/or embryo/fetal risk
	  ▪ Dose adjustments recommended during pregnancy and the postpartum period
	  ▪ Maternal adverse reactions
	  ▪ Fetal/neonatal adverse reactions
	  ▪ Labor or delivery considerations

Data Summary	• When **human data** are available, the label should describe: developmental outcomes, adverse reactions, other adverse effects, types of studies, number of participants and duration of each study, exposure information, and study limitations • When **animal data** are available, the label should describe: types of studies, animal species, dose, duration, and timing of exposure, presence or absence of maternal toxicity, and data limitations

interpret the risks and benefits of medications for individual patients.[1] A consortium of dermatologists published guidance on managing pregnancy-related medication risks for patients with psoriasis in the PLLR era, but to date, similar guidance in other therapeutic areas remains lacking.[3]

Pregnancy Registries

Reports from pregnant women about their experiences with RA drugs are critical for understanding pregnancy-related medication safety, yet few drug labels contain human pregnancy data. In an analysis of 213 new prescription drug approvals between 2003 and 2012, 92.9% of new drug labels contained pregnancy data from animal studies, but only 5.2% had human pregnancy data.[4] Information on breastfeeding safety was even more rare. Overall, nearly half of new drug labels (47.9%) had no breastfeeding data, while 42.7% had animal data and 4.7% had human data.[4]

Pregnancy registries are organized systems for collecting information on medication exposure and pregnancy outcomes, often outside the setting of formal clinical trials. Until recently, however, pregnancy registries have been rare. In the study of new drug approvals between 2003 and 2012, 85% of new medications did not have an associated pregnancy registry.[4] Registry studies that do not focus specifically on pregnancy often overlook this common life event. For example, the Consortium of Rheumatology Researchers of North America (CORRONA) registry collected data on the treatment of 38,337 patients with RA and psoriatic arthritis, yet identified only 251 pregnancies over 10 years of patient observation.[5]

Changes are underway to meet the essential need for better pregnancy-related safety data. With its new drug labeling requirements that prioritize pregnancy registry information, the FDA has signaled the importance of registries in collecting and analyzing pregnancy safety information. Nurses can play a role in strengthening

the body of medication safety evidence by encouraging patients with RA and other diagnoses to participate in pregnancy registries (see associated sidebar at right). In the meantime, the rheumatology community continues to learn from a few key registries that have been collecting pregnancy data and asking important questions for years.

OTIS Registry

The Organization of Teratology Information Specialists (OTIS) Collaborative Research Center launched in 1998 at the University of California at San Diego with a pregnancy registry focused on leflunomide exposure.[6] Over the past 20 years, the project has expanded across the United States and Canada, and now collects data on drugs for immune-mediated diagnoses as well as vaccines, antiviral agents, and asthma medications. The OTIS Research Center works on federally funded projects and industry-sponsored registries.[6]

Using OTIS data collected from thousands of pregnancies, researchers can ask detailed questions about the relationship between RA medications and specific pregnancy outcomes. As an example, one analysis of the OTIS database examined whether biologic therapy during pregnancy increased the risk of opportunistic infections in infants born to mothers with RA.[7]

This particular prospective cohort study was designed to address concerns that biologic therapy might alter infants' postnatal immune function, leading to increased susceptibility to infection. The analysis included 1,184 pregnancies and live births in 3 groups of women: women with RA who were treated with a biologic during pregnancy (n = 252); women with RA who were not treated with a biologic during pregnancy (n = 463); and women who did not have RA (n = 469). After 1 year of post-partum follow-up, there was no statistically significant difference in infection risk across any infant subgroup. Serious or opportunistic infections occurred at the following rates in each subset:[7]

- 2.8% of infants born to women treated with a biologic for RA
- 3.9% of infants born to women not treated with a biologic for RA
- 2.6% of infants born to women without RA

Additional analyses from the OTIS trial have shaped the standards of care for women and

How Nurses Can Participate in RA Registries

Why encourage patients to participate in pregnancy registries? Enrollment in pregnancy registries is voluntary, meaning that women who don't face financial and logistical barriers are more likely to participate. As a result, registry populations tend to be less diverse than real-world clinical practice. Participants disproportionately represent higher socioeconomic and educational levels, which themselves are markers of better pregnancy outcomes. This may skew the results of registry studies and minimize their usefulness as sources of real-world medication safety data.[6] Enrolling more patients, and especially more diverse patients, is critically important to better understand the effects of RA medications on pregnancy and breastfeeding.

Current options for reporting adverse events include the OTIS registry and drug-specific registries sponsored by drug manufacturers. When pregnancy registries are available, the package inserts are required to display the registry contact information in compliance with the new PLLR drug labeling rules. Additional resources for learning more about pregnancy registries include the following:

MotherToBaby is a service of the OTIS initiative that provides patients and clinicians with information on medication safety in pregnancy and breastfeeding, as well as a database of ongoing pregnancy studies. The MotherToBaby website (https://mothertobaby.org/) offers multiple options for support and engagement, including phone, text, email, online chat, and social media groups (Facebook, Twitter, Pinterest, YouTube). Patient education materials are available in English and Spanish. MotherToBaby also maintains a searchable database of pregnancy studies (https://mothertobaby.org/pregnancy-studies/).

The FDA List of Pregnancy Exposure Registries is searchable by medication and medical conditions, such as RA. Current search results point to OTIS studies collecting information on exposure to leflunomide, etanercept, certolizumab, adalimumab, and tofacitinib in pregnant women with RA. (www.fda.gov/ScienceResearch/SpecialTopics/WomensHealthResearch/ucm134848.htm)

men with RA who wish to start a family soon, as well as women who are pregnant or breastfeeding.

National Cohort Studies

Health systems in many countries are structured to function as national registries. In Denmark, researchers have amassed a national database of nearly 2 million children born between 1977 and 2008. The registry database includes 13,556 children exposed to maternal RA and 6,330 children exposed to paternal RA. The Danish database is the source of multiple studies examining pregnancy outcomes and childhood morbidity and mortality in children born to parents with RA.[8-11]

In the Netherlands, the Pregnancy-Induced Amelioration of Rheumatoid Arthritis (PARA) is the largest study of pregnant women with RA. Since its launch in 2002, the ongoing cohort study has collected data on pregnancy-related outcomes in 300 Dutch women with RA.[12]

Disease Activity During Pregnancy

Up to 70% of women with RA will experience a spontaneous improvement in RA symptoms during pregnancy. The degree of improvement, and its effects on RA management, can be highly variable. For 16% to 27% of pregnant women, the improvement is substantial enough to meet the criteria for clinical remission. Despite experiencing some symptomatic relief, however, 50% of women with RA still have active disease during the third trimester of pregnancy.[13]

Multiple studies have tried to explain the beneficial effect of pregnancy in RA, but the exact mechanisms for this phenomenon remain unclear.[14] Hypotheses include the following:

- Suppression of the immune system via human leukocyte antigen incompatibility between woman and fetus
- Changes in maternal blood proteins, with an influx of pregnancy-associated proteins
- Changes to the structure of maternal IgG antibodies due to increased glycosylation
- Shift in maternal T cell population, from a Th1 phenotype to a Th2 phenotype

Naturally, being able to predict the likely RA disease course would be helpful for understanding which pregnant women may improve on their own and which need continued treatment during pregnancy. One recent analysis from the Dutch PARA study examined RA disease activity during 190 pregnancies in 168 women with RA.[13] The goal was to identify factors associated with low disease activity in the third trimester, defined as <3.2 using the Disease Activity Score in 28 joints (DAS28) with C-reactive protein (CRP). In the analysis, 3 clinical factors significantly predicted low RA disease activity in the third trimester:

- Low disease activity (DAS28-CRP<3.2) prior to conception or during the first trimester
- The absence of prednisone use in the first trimester
- The absence of autoantibodies

Of these factors, initial low disease activity was the strongest predictor of clinical status during the third trimester. To be sure, the presence of antibodies and the need for prednisone are themselves markers of more aggressive disease. Even for patients with autoantibodies and a history of prednisone use, however, low DAS28-CRP scores remained significantly associated with low disease activity during the third trimester. These findings underscore the importance of preconception counseling and appropriate treatment to achieve low RA disease activity prior to a planned pregnancy.[13]

RA and Pregnancy Outcomes

National registry studies have been invaluable in helping the medical community understand the effects of RA on pregnancy outcomes and childhood morbidity and mortality.[8-11] Findings from these studies can augment patient counseling for women and men with RA who are interested in starting families.

Preterm Births and Low Birth Weight

RA appears to increase the risk of preterm births, although the impact of RA on overall fetal growth is modest. In the Danish registry study, preterm births were 48% more common among children exposed to maternal RA than among unexposed children (odds ratio, 1.48).[8] Consistent with preterm birth, the mean birthweight of children exposed to maternal RA was 87 gm lower than that of children with no exposure to RA. In addition, the weight of the placenta, on average, was 14 gm lower among children exposed to RA. Despite these differences, children exposed to maternal RA had similar length, head circumference, and abdominal circumference at birth when compared with children born to mothers without RA.[8]

Fathers with RA did not appear to influence these pregnancy endpoints. The study found no association between paternal RA and risk of preterm birth or measures of fetal growth.[8]

Parental RA and Childhood Morbidity

Children who are born to mothers or fathers with RA face an increased risk of several morbidities diagnosed in childhood. During an average of 16 years of follow-up, children in the Danish registry studies were monitored

for the presence of childhood diseases in 11 diagnostic categories. Children with a history of parental RA exposure were significantly more likely than unexposed children to develop diseases in 8 of the 11 categories (Table 3). There was no association between parental RA and the remaining 3 diagnostic categories, which included childhood cancers, benign tumors, or disorders of the circulatory system.[9]

In general, maternal RA exposure contributed to a greater range of childhood diseases—as well as a greater magnitude of increased risk—compared with paternal RA exposure. For instance, relative to children with no parental RA exposure, the risk of childhood respiratory disease was 23% higher for children born to mothers with RA and 9% higher for children whose fathers had RA.[9]

Across all childhood disease categories, the most common individual diagnoses associated with parental RA were autoimmune diseases. Juvenile idiopathic arthritis (JIA), the most prevalent form of arthritis in children, was 3 times more likely to develop in children born to parents with RA than in other children. The risk of type 1 diabetes and asthma were also significantly increased in children born to mothers or fathers with RA. These findings illustrate the strong role of genetics in RA, with children of RA patients inheriting a predisposition for autoimmune disorders.[9]

Another Danish registry study of childhood morbidity focused on the potential link between epilepsy and parental RA. In the analysis, children exposed to maternal RA had a 34% increase in the risk of early childhood epilepsy (onset at age <5 years) and a 26% increase in the risk of late childhood epilepsy (onset at age 5–15 years). However, by the time children reached adolescence (≥15 years), the association between epilepsy and maternal RA exposure disappeared. Furthermore, there was no association between epilepsy at any age and paternal RA.[10]

Based on these findings, Danish researchers suspected that the intrauterine environment might be important to early childhood epilepsy risk and took a second look at the children of mothers with RA. In the second analysis,

Table 3 *Childhood Morbidity and Exposure to Maternal or Paternal RA*[9]

Childhood Diseases	Degree of Significantly Increased Risk in Children with RA Exposure Compared with Unexposed Children	
	Maternal RA	Paternal RA
GENERAL DIAGNOSTIC CATEGORIES		
Endocrine, nutritional, and metabolic diseases	26%	9%
Respiratory disorders	23%	9%
Musculoskeletal and connective tissue disorders	23%	17%
Infections and parasitic disorders	22%	*nonsignificant*
Mental and behavioral disorders	22%	*nonsignificant*
Nervous system and sense organ disorders	20%	8%
Digestive system disorders	16%	6%
Skin and subcutaneous diseases	14%	13%
INDIVIDUAL AUTOIMMUNE DISEASES		
Juvenile idiopathic arthritis	330%	297%
Type 1 diabetes	37%	44%
Asthma	28%	15%

active RA during pregnancy emerged as a critical risk factor. Compared with no RA exposure, the risk of early childhood epilepsy was:

- 90% higher for children exposed to maternal RA in utero
- 26% higher for children born to mothers diagnosed with RA after childbirth

The example of early childhood epilepsy illustrates the complex relationship between parental RA and childhood morbidity. How much of the risk is passed from one generation to the next through genetic predisposition? How much through the intrauterine environment and a cocktail of inflammatory cytokines? Understanding these underlying mechanisms and the potential legacies of RA will enable providers to better counsel their patients.

Parental RA and Childhood Mortality

Despite the increased risk of childhood diseases among children born to parents with RA, there appears to be no link between parental RA and childhood mortality. In a thorough assessment of mortality risk, Danish researchers examined multiple potential signals of increased childhood mortality: 1-year, 3-year, and 5-year mortality, as well as overall mortality, with an average of 16 years of follow-up. Across each measure, there was no difference in mortality between children of parents with RA and those with no history of RA exposure. Furthermore, among individuals who developed respiratory and infectious diseases, the case-fatality rate was similar for all children, regardless of RA exposure.[11]

RA Medication Safety

Achieving optimal control of RA disease activity before and during pregnancy is essential for minimizing the risk of adverse pregnancy outcomes. The challenge for patients and providers is to develop a treatment plan using medications that are compatible with pregnancy. The risks and benefits of different medications may vary based on individual circumstances and should be weighed carefully for each patient.

For detailed information on available RA medications, refer to the enclosed RA Medications and Pregnancy poster.

Biologic DMARDs

Rheumatology providers are becoming more comfortable prescribing biologics to manage inflammatory disease activity in pregnant women. One recent analysis examined trends in medication use in 2,655 pregnant women with RA, psoriatic arthritis, ankylosing spondylitis, or SLE. Between 2001 and 2012, the rate at which women filled prescriptions for biologic agents during pregnancy increased more than 3-fold, from 5.1 to 16.6 per 100 pregnant women.[15] Biologics in this study included abatacept, adalimumab, alefacept (discontinued in 2011), anakinra, certolizumab pegol, etanercept, golimumab, infliximab, natalizumab, rituximab, and tocilizumab.

Anti-TNF Agents

Under the former ABCDX system, anti-TNF agents were Category B agents and considered generally safe in the first and second trimester of pregnancy.[16] According to a recent meta-analysis, women treated with TNF-targeted therapies for immune-mediated diseases such as RA and IBD are more likely than women in the general population to experience spontaneous abortion and preterm birth, and more likely to have low-birth-weight infants.[17] Adverse pregnancy outcomes are, however, likely attributable to the underlying immune-mediated disease rather than its treatment. Pregnancy outcomes are no different for women with RA or IBD receiving anti-TNF agents than for women treated with non-TNF biologics. Furthermore, fetal anomalies are not increased in women treated with anti-TNF agents relative to women in the general population.[17]

An emerging concern regarding TNF-targeted agents involves the placental transfer of the drug to the fetus during the second and third trimesters.[18] The potential for transfer to the fetus depends on the molecular structure of the TNF inhibitor and its ability to bind to placental and fetal Fc receptors.[18]

Monoclonal IgG1 antibodies such as infliximab and adalimumab are more likely to be transported, particularly in the third trimester when fetal IgG1 serum levels are highest.[19] When women are treated with infliximab or adalimumab into the third trimester of pregnancy, placental transfer results in therapeutic levels of anti-TNF in the newborn's cord blood—sometimes at levels that exceed the concentration in the mother's blood.[20,21] By comparison, certolizumab pegol is a pegylated Fc-free antibody fragment that lacks the ability to bind to placental and fetal receptors.[19] When women are treated with certolizumab pegol into the third trimester, anti-TNF drug levels are below the threshold of detection in newborn cord blood.[22] In the future, certolizumab pegol may have a preferred role for women who require anti-TNF therapy into the third trimester. Until new standards of care are defined, however, discontinuing anti-TNF therapy by gestational week 20 is advised.[18]

Non-TNF Biologics

Limited pregnancy safety data are available for the non-TNF biologics. Anakinra was rated as Category B, while abatacept, rituximab, and tocilizumab were classified as Category C medications.[16] Data from small studies indicate no increased risk of adverse pregnancy outcomes in women taking non-TNF biologics (abatacept, n=3; rituximab, n=3; tocilizumab, n=5), but the numbers remain too small for definitive conclusions.[23]

Sarilumab is the second interleukin (IL)-6 inhibitor available for RA treatment after its approval in May 2017,

well after the PLLR effective date of June 2015. As such, sarilumab is the first agent available for the treatment of RA without a former ABCDX category.

Small Molecule Inhibitors

Tofacitinib, a small molecule JAK inhibitor, was approved as a Category C drug.[16] One study examined pregnancy outcomes among women of childbearing age who enrolled in clinical trials of tofacitinib for RA or psoriasis (n=1,821).[24] The analysis included 47 women who became pregnant while receiving tofacitinib alone or in combination with MTX. All pregnancy outcomes among the tofacitinib-treated women were consistent with those expected in the general population: 25 healthy live births, 8 medical terminations, 7 spontaneous abortions, 1 case of congenital pulmonary valve stenosis, and 6 pending or lost-to-follow-up cases.[24]

Synthetic DMARDs

Synthetic DMARDs range from agents that are contradicted during pregnancy to those that are preferred medications for women with RA who require treatment during pregnancy. As a Category X agent in the former rating system, ***methotrexate*** is contraindicated during pregnancy and breastfeeding. Concerns include an increased risk of spontaneous abortion and fetal abnormalities affecting the heart, central nervous system, and skeleton.[25] When a pregnancy is planned, MTX should be discontinued prior to conception. Patients of childbearing potential should be counseled about the importance of effective birth control while taking MTX.[25]

Women who discover that they are pregnant while still taking MTX, or who have an accidental MTX exposure near the time of conception, should be reassured that MTX exposure does not necessarily result in an adverse outcome. One analysis of the OTIS database examined 136 pregnancies involving MTX exposure within 12 weeks of conception and 188 pregnancies involving MTX exposure after conception (median exposure time, 4.3 weeks after the last menstrual cycle).[26] Post-conception MTX exposure resulted in a high rate of spontaneous abortion (42.5%) and an increase in the rate of major birth defects relative to pregnancies in women with RA and no MTX exposure (6.6% vs. 3.9%, respectively). Among pregnancies with a preconception MTX exposure, the rates of spontaneous abortion and major birth defects were comparable to those observed in pregnant women with RA. These findings can inform patient counseling following an inadvertent MTX exposure for women who are concerned about their pregnancies.[25] According to current standards of care, patients should be advised that there is no dose of MTX low enough to be safely incorporated into RA treatment plans for pregnant women.[25]

Similar to MTX, ***leflunomide*** is contraindicated in pregnancy (Category X) as well as in patients who wish to start a family in the near future. Given the long half-life of leflunomide, an 11-day course of cholestyramine is recommended for both male and female patients to completely remove the DMARD from the system before trying to conceive.[27] Blood testing is required to confirm that leflunomide has been eliminated.[27]

Hydroxychloroquine (HCQ) is one of the most commonly used DMARDs in women with RA who require treatment during pregnancy.[15] The safety of HCQ during pregnancy has been studied most widely in women with SLE and connective tissue disorders.[28,29] Under the ABCDX rating system, HCQ was classified as a Category C medication.[25]

Formerly classified as a Category B drug, ***sulfasalazine*** is considered safe for continued use throughout pregnancy in women with RA.[25] Data supporting the safety of sulfasalazine come largely from patients with Crohn's disease and IBD, who have a history of sulfasalazine use with no increased risk of adverse pregnancy outcomes.[30,31] Women who are taking sulfasalazine should also take 1 mg of oral folic acid twice daily during the 3 months prior to conception and during pregnancy to avoid the risk of fetal neural tube defects.[32]

Postpartum RA Management

Parenting can be challenging during the postpartum period for all women, but especially for patients who are affected by RA disease flares. Patient counseling is essential so that women and their partners know what to expect after childbirth (see "What to Expect When You're a New Parent With RA" essay later in this issue for more information). Postpartum RA treatment choices are limited for women who wish to breastfeed, so it is important to have a plan in place to manage postpartum disease activity. For example, it may be helpful to educate women about how to prevent overuse of inflamed joints as they care for their newborns.[33]

Postpartum Flares

After a period of decreased RA disease activity during pregnancy, disease flares are common in the postpartum period. In one study of postpartum RA disease activity, 36% of women had a moderate flare and an additional 4% of women had a severe flare.[14] For all women in the study (n=84), the mean DAS28 score increased by 0.30 points, from 3.5 to 3.8, between postpartum weeks 6 and 12. By postpartum week 26, the mean DAS28 scores stabilized and returned to pre-pregnancy levels.[14]

Some evidence suggests that breastfeeding may trigger a postpartum RA disease flare, especially after a first pregnancy.[34] One study of 137 women with RA included 38 women who were breastfeeding following their first pregnancy, 50 women who were repeat breast-feeders (i.e., they breastfed after prior pregnancies), and 49 women who did not breastfeed. At 6 months postpartum, women who were first-time breast-feeders had more severe joint pain and a greater number of swollen/tender joints than the other groups of women. One explanation for this finding involves prolactin, a proinflammatory hormone that is necessary for breastfeeding. It is unclear, however, why women who

Table 4 *Medications for Women with RA who are Breastfeeding*[25]

Preferred medications *(if treatment is required)*	Insufficient evidence to support safe use	Contraindicated medications
Glucocorticoids NSAIDs Hydroxychloroquine Sulfasalazine	Anti-TNF agents Anakinra Rituximab Tocilizumab Tofacitinib	Methotrexate Leflunomide Azathioprine

were breastfeeding after their first pregnancies, and not those with a history of breastfeeding, were particularly susceptible to increased RA disease activity at 6 months postpartum.[34]

Breastfeeding Considerations

Medications are considered compatible with breastfeeding when they do not adversely affect the production of breast milk and cause no harm to the nursing infant. Glucocorticoids, nonsteroidal antiinflammatory drugs (NSAIDs), HCQ, and sulfasalazine are the preferred medications for women with RA who require treatment while breastfeeding (Table 4).[25] In contrast, MTX, leflunomide, and azathioprine are contraindicated for breastfeeding women with RA.[25]

Women who experience flares while breastfeeding may need to adjust their RA treatment regimen. The LactMed database (toxnet.nlm.nih.gov/newtoxnet/lactmed.htm) is a free online database maintained by the National Library of Medicine with information on drug safety in lactation for more than 450 medications. Search results include information on drug levels in breast milk and in infant blood, the American Academy of Pediatrics categories regarding the compatibility of medications with breastfeeding, and alterative medications to consider for women who are breastfeeding.[35]

Under the PLLR system, Section 2.1 of all medications labels should contain a summary of known precautions and recommendations related to breastfeeding. Data may include the concentration of active drug metabolites in breast milk, serum drug levels in breastfeeding infants, the pharmacokinetics of drug metabolism and excretion in the milk, and recommendations on optimal timing of breastfeeding to minimize infant drug exposure.

How Are We Doing? RA Treatment and Medication Counseling Patterns

Real-world treatment trends are important for understanding gaps in care. One recent study evaluated 990 women with RA who received immunomodulatory agents during the 3 months prior to conception and had a pregnancy that resulted in a live birth.[15] Findings showed high rates of medication use during the preconception period, including 14.9% of patients who were taking MTX prior to getting pregnant (Table 5). Most patients tapered off MTX and biologic DMARDs by the second and third trimester. In the third trimester, however, 19.5% of patients continued to use systemic steroids (prednisone, hydrocortisone, cortisone, prednisolone, methylprednisolone, dexamethasone, triamcinolone, or betamethasone).[15]

Table 5 *Real-World RA Drug Use Patterns Before and During Pregnancy*[15]

Medications	3 Months Prior to Conception	First Trimester	Second Trimester	Third Trimester
Steroids	60.4%	25.1%	21.7%	19.5%
Hydroxychloroquine	19.5%	7.5%	2.5%	2.3%
Etanercept	17.0%	6.5%	2.5%	2.0%
Methotrexate	14.9%	2.3%	0.1%	0.2%
Adalimumab	8.1%	4.2%	1.4%	1.0%

Lack of Preconception Counseling

Preconception counseling in the primary care setting is inadequate, leaving patients vulnerable to poor treatment choices before and during pregnancy. In one study of 801 women aged 18 to 50 years attending primary care clinics, 27% were prescribed medications with potential teratogenic effects. Of these patients, 43% did not receive counseling regarding the risk of medication-related birth defects or the importance of contraception during treatment.[36] Patients with female providers were twice as likely to have received counseling than patients with male providers, suggesting the presence of stigma, awkwardness, or other gender-based barriers to contraceptive counseling. The effort to provide counseling was worthwhile; women who received counseling were more likely to use contraception after being prescribed a teratogenic medication than women who did not receive any counseling.[36]

Another study examined more than 1 million prescriptions filled by 488,175 women aged 15 to 44 years within the Kaiser Permanente Northern California health system.[37] In this analysis, 1 in 6 women of childbearing age filled a prescription for a Class D or X teratogenic medication.[37] Of these, only half (48%) received any contraceptive counseling.[37] Furthermore, among those who filled a prescription for a teratogenic medication, approximately 1% had a documented pregnancy within 3 months.[37] Together, these findings show that women of childbearing potential are not receiving counseling about medication safety from their primary care providers.

What About the Dads?

Men with RA should undergo preconception counseling to decrease the risk of treatment-related fertility issues and to understand the potential implications of their disease for their children. As described in the RA and Pregnancy Outcomes section earlier in this issue, paternal RA does not increase the risk of preterm birth or adversely affect fetal growth.[8] Genetic risk factors are inescapable, however, and fathers with RA appear to contribute to an increased risk of immune-mediate diseases such as JIA, type 1 diabetes, and asthma (Table 3).[8]

Men with RA can successfully start a family with minor (if any) RA treatment adjustments. Table 6 summarizes general guidance for medication management and family planning considerations for men with RA.[25]

Table 6 *Medication Management and Family Planning Considerations for Men with RA*[25]

Drug	Considerations
Methotrexate	Hold for 3 months prior to attempted conception
Sulfasalazine	Consider holding in men who may have issues with fertility
Azathioprine	No data to suggest adverse outcomes
Leflunomide	Limited data, but no adverse outcomes reported
TNF inhibitors	May disrupt sperm production, but generally favorable outcomes
Rituximab	Limited data, but adverse outcomes reported
Abatacept	Limited data, but adverse outcomes reported

Based on evidence that methotrexate may disrupt sperm production, some experts recommend holding methotrexate for 3 months—long enough to wash out one spermatogenic cycle (74 days)—prior to planned conception.[25] Other agents such as sulfasalazine may also impair fertility, although the evidence to guide their use is less robust.[25] As drug labels transition to the PLLR system, Section 8.3 will include considerations for male and female patients of childbearing potential. Importantly, this section will summarize available evidence and recommendations on contraception and infertility.

Summary

Preconception counseling is an essential starting point for patients with RA who are interested in starting a family. Developing a treatment plan with medications that are compatible with fertility, pregnancy, and breastfeeding can be challenging, especially during the transition to the PLLR era. Compared with ABCDX ratings, the new drug labeling requirements shift the burden onto providers to consider a greater volume of information about medication safety. Once a treatment plan has been developed, both men and women with RA should be encouraged to participate in pregnancy registries if feasible. Throughout treatment, maintaining RA disease control must be carefully balanced against the potential for adverse pregnancy and postpartum outcomes. Together, patients and providers can make evidence-based decisions about RA care that increase the likelihood of a healthy pregnancy.

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When Our Patients Know What is Best

by Jacqueline Fritz, RN, MSN, CNS, RN-BC

As indicated within this issue of *Rheumatology Nurse Practice*, there is specific guidance that providers must be mindful of when caring for a patient of childbearing age who has been diagnosed with rheumatoid arthritis (RA). Whenever I hear, "Can I have a baby?" from one of these patients, my radar immediately perks up.

Of course, the initial considerations surround the use of contraindicated drugs such as methotrexate and leflunomide during the pre-conception period. My practice's electronic medical record even has a section where we must indicate whether we have discussed contraindicated drugs during pregnancy in women of childbearing age to ensure that the topic is never overlooked.

Once pregnancy is confirmed, many patients will see their disease activity improve significantly due to an increase in cortisol levels,[1] although for some women, their RA will remain active or even flare during pregnancy. These can be complicated patients to manage as we try to balance the patient's disease activity in addition to the baby's health.

And then there are those patients in whom there is an extra layer of complexity that is, at least to some degree, beyond our control.

One of my patients, MD, is a 39-year family physician (note the irony of her initials). She comes from a family of practicing physicians who unfortunately all share the burden of having RA. MD's RA is very active—18 months ago, she had a C-reactive protein of 37.5 mg/L, rheumatoid factor (RF) IgM of 128 IU/mL, and RF IgA of 354 IU/mL. She also had small bilateral ulnar erosions and a joint count of 8 tender and 6 swollen joints. Typically, MD reports morning stiffness of approximately 45 minutes.

Managing MD's RA has been a challenge. She has tried and failed a barrage of biologics, with a failed history of infliximab, tofacitinib, adalimumab, certolizumab pegol, tocilizumab, and abatacept. She has had trouble with non-biologics as well, as hydroxychloroquine caused darkening of the skin and she could not tolerate indomethacin. Up until a year ago, MD was somewhat stable on a regimen of prednisone 12.5 mg/d, meloxicam 7.5 mg BID and intravenous golimumab 150 mg every other month.

Last year, MD came in and told me that she and her husband wanted to try for a third child (they have a 6-year-old daughter and 4-year-old son). I immediately warned her that, with her RA being so active, pregnancy

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"Learning new information, even information brought to us by our patients, is what makes our job so challenging and often so rewarding"

was going to be difficult. MD said that she understood the risks of her decision, but that she nonetheless was adamant in her desire of another child. And so, in light of two recent failed IVF procedures and two miscarriages, we agreed to try to help her have a successful pregnancy.

Our first step was to see about a substitute for prednisone, but repository corticotropin injections were too costly, so we maintained the corticosteroid. This is an atypical decision in our practice given the potential side effects of prednisone, but both we and MD felt this would be the most appropriate decision in light of her disease activity.

MD was insistent that, based on her independent research, controlling her inflammation would be the key to a successful pregnancy. There is indeed some research supporting this theory. A 2015 study by Comba et al showed that increased blood and/or tissue levels of several upregulated cytokines, including IL-18, IL-12, IFN-y, and ICAM-1 may be associated with recurrent pregnancy loss.[2] Armed with data from this study, MD felt it was important to maintain a stable dose of prednisone as she attempted to get and then remain pregnant.

Fortunately, this story will apparently have a happy ending. MD was able to get pregnant and maintain the pregnancy with manageable side effects. She is now in her 37th week of pregnancy and is scheduled for a C-section.

With easy online access to both good and bad information, our patients often come armed with reams of data that we have to sit down and discuss with them. It is simply part of being a healthcare provider in the 21st century. Learning new information, even information brought to us by our patients, is what makes our job so challenging and often so rewarding.

Sharing the pregnancy journey with MD has been, at times, perilous, but looks to be ending with what she hoped for—another healthy, happy baby.

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What to Expect When You're a New Parent With RA

by Elizabeth Kirchner, CNP, RN-BC

Being a new parent is never easy, but it can be especially challenging for patients with a chronic disease such as rheumatoid arthritis (RA). Here are some tips I have given to my patients with RA over the years—I hope you find them helpful for use in your practice!

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1. Let's get the big question out of the way first: Breastfeeding. Depending on what medications mom is on, breastfeeding *may* be safe for the baby. Breastfeeding can be wonderful for a number of reasons that I won't go into here. However, for a new mom with RA, breastfeeding might not be the best choice. I tell my new moms to consider that they need their sleep in order to help keep their RA under control and that they cannot get an adequate amount of quality sleep if they are the only ones feeding the baby every 2-4 hours. I typically encourage them to consider pumping and storing so that another adult can take some of the night shift.

It's also important to remind new moms that the world won't end if formula ends up being the best choice for the patient and her family. I tell my patients to carefully consider the pros and cons of every option and come up with what works for them.

2. While we're on the topic of rest: I tell my patients to get enough! They need to accept help when it is offered, and ask for it when it isn't. Every chore or task the new parent doesn't have to complete means more energy to take care of him or herself and the baby. So when the neighbor offers to bring dinner over or a sibling offers to come over to do laundry, a hearty "Yes, please!" is the correct answer.

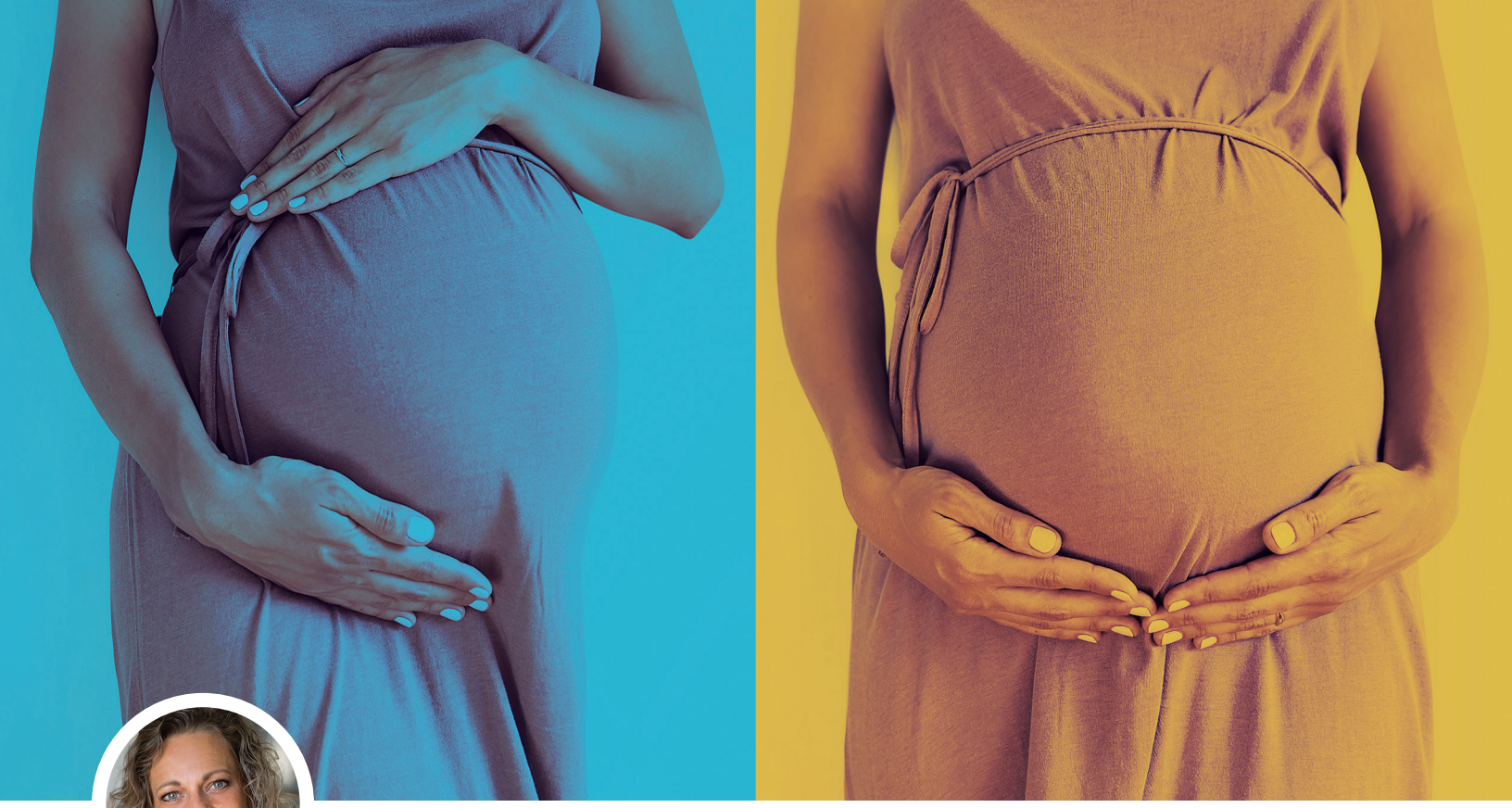
3. New parents need to be especially careful about staying hydrated. As silly as it sounds, sometimes the basic things are the first to get lost in the shuffle of new parenthood. Dehydration can make joint pains worse, and nobody wants that.

4. As much as possible, try to stay on a schedule for eating (I'm talking about the new parents here, not the baby!). This not only helps with overall health, but it can counteract some of the effects of the inevitable sleep deprivation that occurs.

5. If mom is the one with the RA, I remind her that RA may naturally be less active during pregnancy, so be on the lookout for symptoms to return post-partum. Waiting for a full-fledged flare will just make it harder to get her disease under control; patients need to call at the first sign of increased disease activity.

6. This isn't specific to RA but is important for ***every*** new mom so I make sure to bring it up: Postpartum depression (PPD) is real, it is not just "baby blues," and it is NOT a sign of not being "cut out" for motherhood. I remind my patients of the signs and symptoms of PPD and urge them to contact their OB/GYN if they have them.

7. Last but not least—relax and enjoy! The days when baby spits up on your clothes five times in a row and decides that napping is optional are tough, but blink… and that baby is off to her first day of kindergarten. Savor the moments (even the vomit-filled ones)!



A Tale of Two Pregnancies

by Iris Zink, MSN, NP, RN-BC

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As rheumatology nurses, we see many patients in what should be the prime years of their lives. In their 20s or 30s, I currently have numerous recently married women in my practice as patients who have a new diagnosis of rheumatoid arthritis (RA), dealing them a crushing blow just as they are starting to think about starting a family.

Fortunately, we have come a long way in the last two decades and gained considerable experience with both biologic and nonbiologic disease modifying antirheumatic drugs (DMARDs), making what was once a harrowing journey into pregnancy something much more manageable. There are still valuable lessons, though, that we can learn from our early experiences with biologic DMARDs.

One of my patients from early in my nursing career, CS, was diagnosed with juvenile RA as a 3-year-old. As she entered her mid-20s, she started to think about starting a family. While her rheumatologist initially suggested that CS discontinue all medications except for prednisone, CS' disease activity was too significant for her to comply with his suggestion and she continued on etanercept until she indeed became pregnant in 1999.

CS was among our lucky RA patients whose disease goes into clinical remission during pregnancy, although her disease came screaming back shortly after giving birth to a healthy son. CS' lactation consultant informed her that it was OK to go back on etanercept while breastfeeding her newborn, but her rheumatologist disagreed, telling her that should only go back on the drug if she stopped breastfeeding. She continued the etanercept while breastfeeding and trusted her lactation consultant.

Three years later, CS decided it was time to try for a second child. This time, she stopped taking etanercept once she began trying to become pregnant, Unfortunately, she suffered a miscarriage, and her RA spiraled out of control. Every few weeks, she came in to have 50 cc of fluid or more aspirated from her swollen knees, ankles, and wrists. After a few months, CS was worn down, ready to give up on her hopes of having another child so that she could restart her biologic.

Unfortunately, in 2002, there was a national shortage of etanercept, and CS' rheumatology team could not get her access to the drug. It was a rough few weeks, but CS finally was able to restart etanercept once the shortage resolved and she became pregnant soon after getting access to the biologic. Her second pregnancy, unfortunately, was not as kind to her disease as the first, and CS chose to stay on etanercept throughout the pregnancy and during her months of breastfeeding.

Fortunately, there were no drug-related health issues with either of CS' children. At the time of her pregnancies, that was still a significant concern in rheumatology, although with experience, we are no longer as reticent to keep our patients on biologic therapy as we once were.

Another patient I remember from early in my rheumatology nursing career was LW, a woman with RA in her late 20s who was being treated with methotrexate in 2003. LW was on birth control, as we always recommend for our sexually-active patients taking methotrexate. Due to advancing disease, LW was referred to orthopedics for wrist fusion surgery. We held her methotrexate in the 2 weeks before the surgery. Unfortunately, her recovery was complicated by a post-surgical infection that required antibiotics. The infection soon resolved, but we think that the antibiotics affected her birth control, and LW became pregnant.

As with CS, LW's disease went into remission during pregnancy without any medication, and it remained that way until she began to wean her son from breast feeding. At that point, CS' RA returned worse than ever, to the point where she said she was having trouble with the day-to-day care of her son. We started CS on adalimumab to get her disease under control.

Eight years later, while on abatacept, LW became pregnant for a second time. She stopped the biologic after learning of the pregnancy and again was fortunate that her disease went into remission during her pregnancy (she wasn't the first nor the last patient to tell me that she wished she could feel the way she felt when she was pregnant all the time).

LW's disease again flared when she discontinued breastfeeding and did not improve even with the restart of abatacept. She was switched to etanercept, which has successfully kept her in remission for the last few years.

So then what did I learn from these two patients?

1. **It is difficult for our patients to get pregnant when their RA is active.** Yes, there are potential risks in keeping a patient on biologic therapy as they try to get pregnant, but we are learning with more and more experience that, fortunately, these risks are relatively low. Today, I typically try to keep my RA patients on biologic therapy until they become pregnant and only then taper or stop the medication if their disease remains in remission during pregnancy.
2. **Unplanned pregnancies can happen anytime, even when our patients are on birth control.** At my current practice, we have our female patients of childbearing age sign a "Pregnancy Pact" if they are being treated with either methotrexate or leflunomide to reinforce the dangers of these medications on the fetus. It helps get the message across, but is obviously not a foolproof guarantee.
3. **As rheumatology nurses, we do not have all the answers.** Talking about family planning adds time and complexity as we treat patients with autoimmune diseases, but it is necessary in any holistic approach to disease management.
4. **Trust your patients.** I have pictures of both CS and LW in my office with their babies. When I have a young woman with RA who is considering becoming pregnant, I show them the pictures to reassure them that "We can do this together and safely."

None of our patients should be discouraged from starting a family. It is our job to support and educate, and to make sure our patients know that we care about them as individuals. We have the tools in our treatment arsenal to keep our patients' babies safe while also reining in their disease activity. In some cases, it can be a tricky risk/benefit balance, but there are so many happy memories in my career from helping women with RA have a successful pregnancy. There are few things that have been more personally rewarding.

THE **PATIENT** PERSPECTIVE

What I Wish My Rheumatology Team Had Told Me Before I Got Pregnant

by Mariah Zebrowski Leach

When I was diagnosed with rheumatoid arthritis (RA) at the age of 25, one of my first concerns was how it would impact my ability to start a family. Though I was lucky to have an extremely supportive rheumatology team, I still felt there was an acute lack of information and resources available about this topic. I ended up feeling very alone and confused as I made difficult decisions about my family's future.

Today, I am fortunate to have two little boys—ages 5 and 3—and a little girl on the way! In the hopes that other women will not have to feel as alone as I did, I run a Facebook support group for moms with chronic illnesses called Mamas Facing Forward. We have almost 600 members from all over the world, most of whom live with RA.

To get a sense of issues our members wished their rheumatology teams had told them when they were first considering pregnancy, I asked some of them to share their experiences and advice. Here is what I found out.

The Impact of NSAIDs on Ovulation

I didn't learn about the potential impact of NSAIDs on ovulation until after my first two pregnancies (their use has been shown to inhibit ovulation and reduce progesterone levels in young women, which may undermine fertility[1]). When I found out about this link through my own education, I was shocked. I had carefully discussed my desire to get pregnant since the time of my RA diagnosis, but the impact of NSAIDs on fertility was never mentioned during a discussion of medication options. I wasn't the only one who had this issue.

"I had taken NSAIDs for over 30 years, yet none of my doctors ever told me (about their impact on fertility)," shared Christina, mom to a 5- and 3-year-old.

TAKEAWAY: *Patients need to know which medications—including over-the-counter options—are safe to use for symptom relief without impacting our conception chances.*

How to Manage Conflicting Advice

Perhaps the most common issue I hear from women with RA who are considering becoming pregnant is the difficulty they have resolving conflicting advice from various clinicians, especially when it comes to medication safety. More often than not, these clinicians never communicate directly with each other, forcing us to act as "middle men" who then need to make complicated and stressful decisions without clear advice.

"I wish I had been cared for holistically by a team of advocates vs. each physician working in his own silo," said Jeanmarie, mom to a 6- and 1-year-old.

Lindsay, mom to a 4- and 1-year-old, even came to a visit prepared with research to support medication use during breastfeeding, but her rheumatologist wouldn't even look at it.

"As a result, I breastfed without medication and flared to the point of not being able to pick my baby up," she said. "I finally gave up breastfeeding. I felt like a failure and suffered from postpartum depression."

TAKEAWAY: *Talk to your patients about the advice they are getting from their entire healthcare team and help them sort through the confusion.*

The Truth About Pregnancy Remission

I know from personal experience that remission during pregnancy is not a guarantee, but I'm not the

AUTHOR BIO

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only woman who was led to believe that worsening of disease activity is highly unlikely during pregnancy.

"The two worst flares of my life were during pregnancy, and I was completely unprepared (and entirely unmedicated) the first time," shared Kimberly, mom to a 2-year-old and 3-month-old.

"I had dreamed of this magical time when there was no medicine and no pain," concurred Casey, mom to a 1-year-old. "I wish someone would have been honest with me."

TAKEAWAY: *Don't unnecessarily inflate your patient's hopes as they consider becoming pregnant. It's fine to tell them that some women will see their RA symptoms get significantly better during pregnancy, but be cautious about overpromising.*

Prepare Us For Postpartum Challenges

After my own pregnancies, I know the likelihood of a postpartum RA flare is high, so this time around I'm planning accordingly. After my first pregnancy, I, like many others, wasn't nearly as ready.

"I wish my team would have sat me down, warned that a flare was likely, and (explained) what that would look like," agreed Stephanie, mom to a 2-year-old.

Cheryl, mom to a 3-year-old, added that she wishes she had been told that her body might not respond as well postpartum as it had previously to the same biologic.

Several moms also said they would have liked advice on how to physically care for a new baby without putting additional stress on their joints.

"We wasted a lot of money, time, and anxiety trying to figure out which baby gear was 'RA friendly' so I could feel like a competent mother," said Erin, mom to a 12- and 9-year-old. "Empowerment would have been a great thing to get from a healthcare professional. To have them say, 'You can do this well, and here's how.'"

Almost all the moms I heard from agreed that they would have liked to be connected to other patients or online support forums so they could discuss their issues with women who have had similar first-hand experiences and could understand their problems.

TAKEAWAY: *The finish line for women with RA isn't the delivery of a healthy baby. For many, the immediate postpartum period is the most challenging part of the journey. Setting up a postpartum flare plan with your patients prior to delivery is often a good idea, especially with the overwhelming responsibilities of a new baby.*

So what do I hope that the rheumatology nursing community learns from what I heard from moms with RA? I think the most important things we need from our rheumatology team when considering pregnancy are encouragement, support, and information. We need to know that you are "on our team," and we need to know what all of our options are before, during, and after pregnancy. That way, we can work together to create the best possible plan to turn our dreams of motherhood into a reality.

Reference

1. Salman S. Non-steroidal anti-inflammatory drugs inhibit ovulation after just ten days. EULAR 2015. Abstract OP0131.

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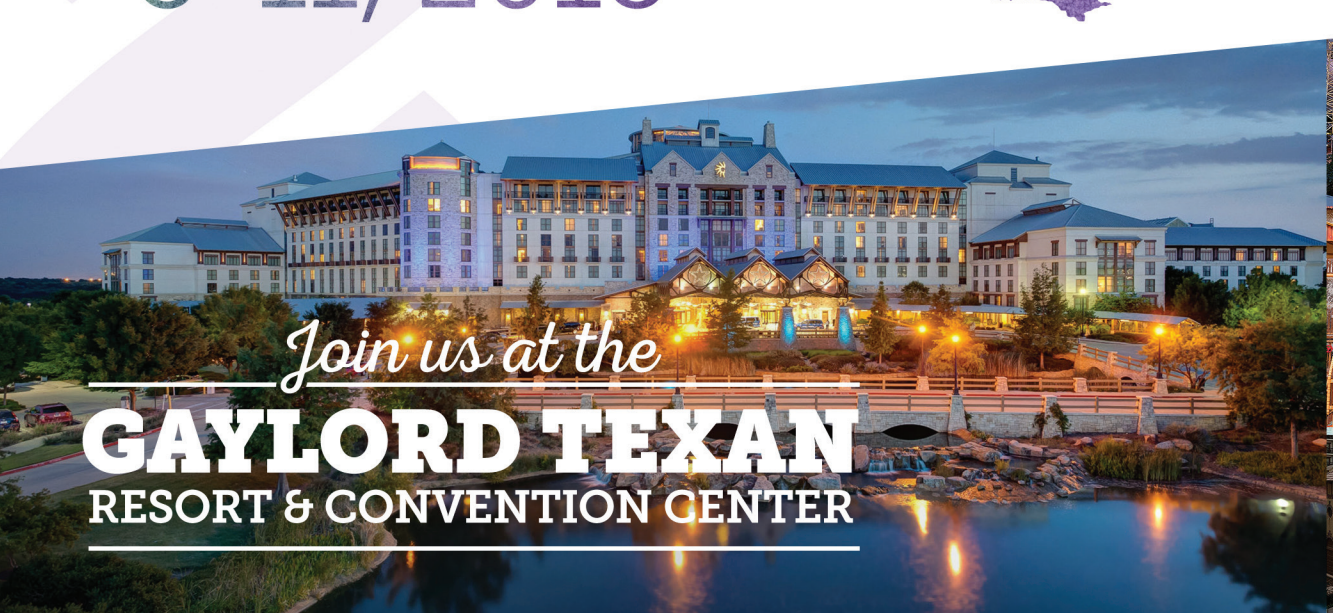

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