Pregnancy and Women's Health in the Rheumatic Diseases

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Disclosures

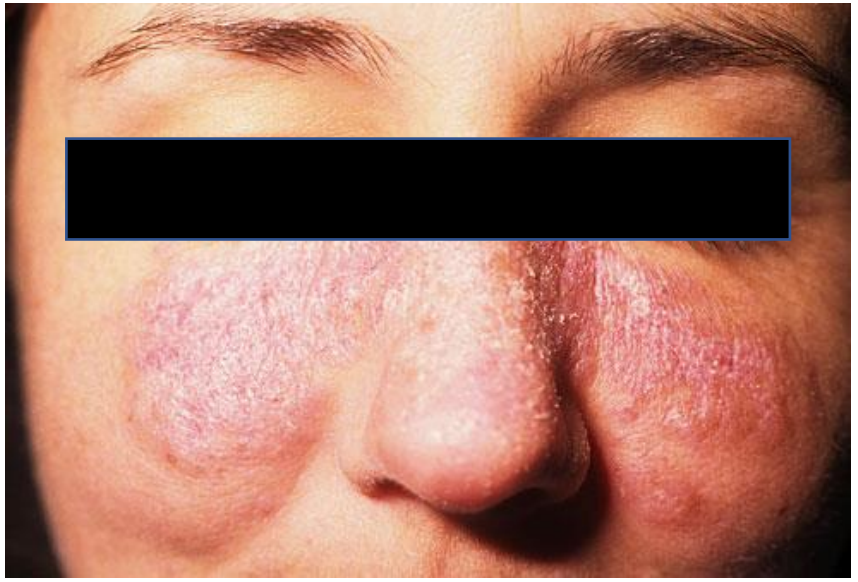
Nothing to disclose

Objectives

- Recognize that pregnancy and women's health in the rheumatic diseases require a coordinated and interdisciplinary approach
- Acknowledge and consider a woman's reproductive journey with her diagnosis and treatment decisions
- Review the latest American College of Rheumatology Guidelines
- Optimize care with shared decision-making during family planning, pregnancy, breast-feeding, and the post-partum period

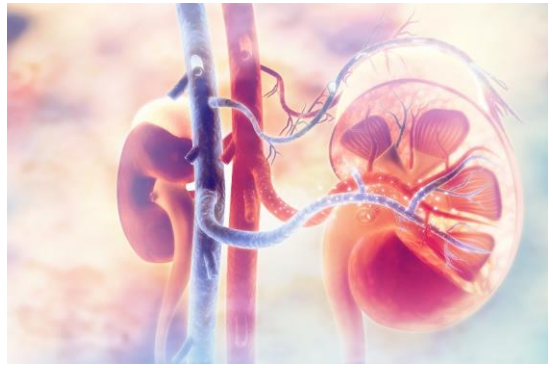
Patient case

- RW – 36 year old Asian female with SLE
- Diagnosed with systemic lupus erythematosus at age 18 following a camping trip in the Catskill Mountains, NY
  - Symptoms of malar rash, headaches, fever, syncope, acute renal failure
- Treated with prolonged steroids, hydroxychloroquine, mycophenolate mofetil, azathioprine
- Married at age 31
- Pregnant at age 33



Patient case

- Premature birth at 27 weeks gestation with severe, life-threatening complications for both the baby and the patient
- Progressed to end-stage renal disease requiring hemodialysis and treatment with high-dose steroids and cyclophosphamide
- Status post renal transplant at age 39
- Treated with multiple immunosuppressive medications lifelong



Patient case

- Expresses desire for 2nd child at age 36

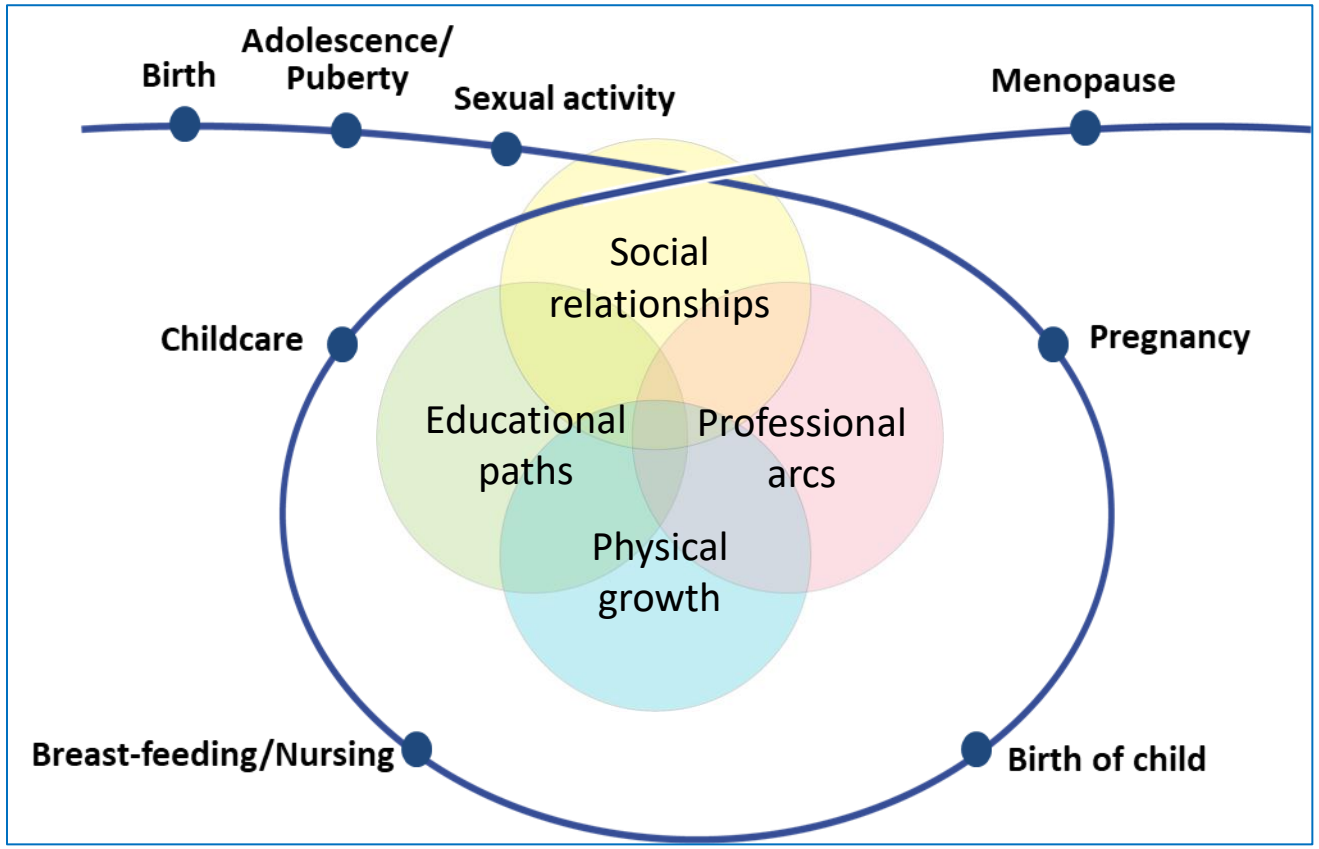
Patient case

What would you recommend?

Scope

- Autoimmune diseases affect ~5-8% of the US population → 16-26 million[1]
- 78% of patients with an autoimmune disease are women → 12-18 million[1]
- Approximately 1 in 5 patients with rheumatic diseases are women of childbearing age (between the ages of 18-45) → 2.4-3.6 million
- Women with rheumatic diseases represent an important subpopulation
- Every woman experiences a reproductive journey

A Woman's Reproductive Journey



- From menarche to menopause, thus lasting ~29-45 years
- May be linear or a carousel
  - A woman in the US has 1.8 children in her lifetime
- Concomitant journeys
  - Relationships, educational path, professional arcs, physical growth and other medical issues

Hormonal flux and autoimmune disease

- Hypothesis that hormones may be the basis of autoimmune disease[3]
  - 78% of patients with autoimmune diseases are women
- Some women with rheumatic diseases report flares of their disease with menstrual cycles, while others experience alleviation of symptoms[4]
- Women with inflammatory bowel disease may experience exacerbation of GI symptoms during menses[5]
- Higher levels of estrogen may improve psoriasis[6]

THEREFORE, ASK! (How are your symptoms during menstruation?)

ASK !!! Patients may have questions…

- What is my diagnosis?
- How will I be treated?
- Can I afford the treatments?
- Will I still be able to work or go to school?
- Will I become disabled?
- How will this affect my relationships?
- Can I have children?
- How will others think of me and my disease? (Concept of disclosure)
- Is there hope?

OUR GOAL SHOULD BE TO TREAT THE PATIENT, NOT JUST THE DISEASE

Asking leads to patient-centered care

- Asking open-ended questions is the best way to get to know patients, establish rapport, and build trust
- Understanding patient concerns is essential for establishing expectations and achieving disease control
- Ultimate goal is for patients to achieve remission, to lead a full and active life

CHANGE THE PARADIGM FROM A PROVIDER-CENTERED APPROACH TO A PATIENT-CENTERED FOCUS

If remission isn't achieved, autoimmune disease can cause substantial burdens

In the home, the woman is usually the primary caretaker of the family

Death

Increased costs

Stress, depression

Work productivity

Social impairment

Functional disability

Disease progression

Fatigue, decreased energy

Sexual health and pregnancy in the rheumatic diseases

Sexual Health

- Sexual health: “A state of physical, mental, and social well-being in relation to sexuality[7]”
- Autoimmune disease can negatively impact a woman’s sexual health

“ I’m so tired, I just don’t want to have sex.”

“ My psoriasis is embarrassing. It makes it hard to get close to someone.”

“ Arthritis makes by entire body hurt—the last thing I want is sex.”

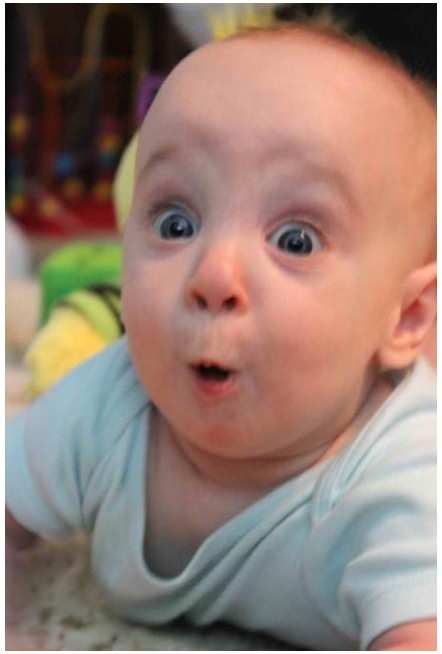
“ I can’t have a boyfriend with an ostomy.”

It takes a village…

A comprehensive health care team can support sexual health in women with autoimmune diseases

Considerations of family planning and pregnancy

- ~50% of pregnancies in the US are unplanned[8]
- Most women discover that they are pregnant 2-5 weeks after conception[9]
- Development of the major organs of the fetus begins the 3rd week after conception[10]
- Therefore, family planning should be addressed in all women of reproductive age



“Have you thought about when you’d like to start a family?”

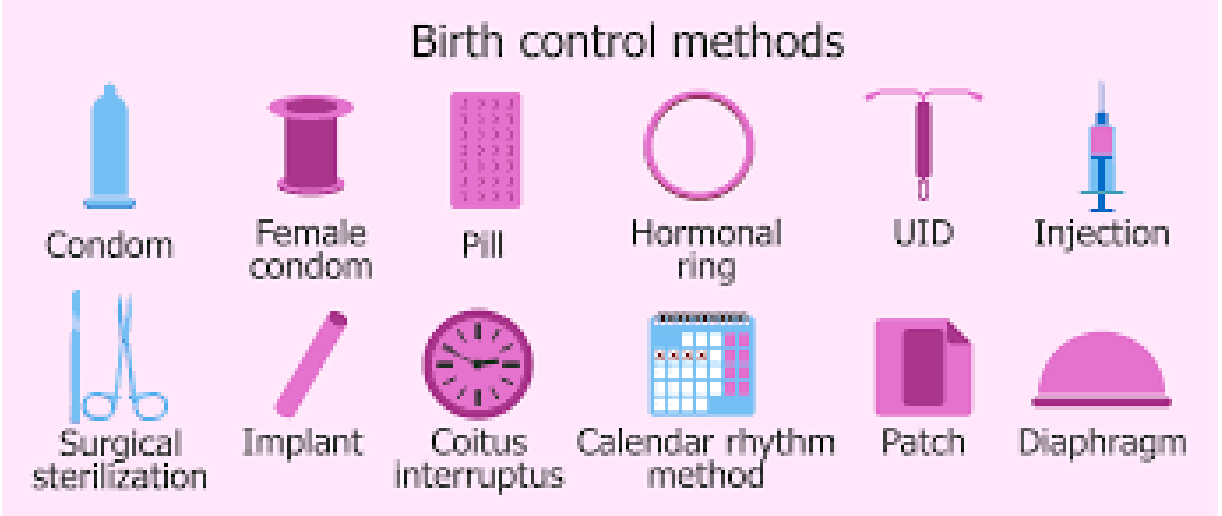
Considerations of family planning and pregnancy

- Some medications may impact fertility and/or may be teratogenic
  - Cyclophosphamide
  - Methotrexate
  - Leflunomide
  - Mycophenolate mofetil
  - Belimumab
  - JAK inhibitors
  - Sulfasalazine
  - Acitretin
  - Thalidomide
  - Tazarotene

Birth control considerations

- If ~50% of pregnancies are unplanned and several medications may have adverse events, then it is essential to discuss family planning and birth control with patients

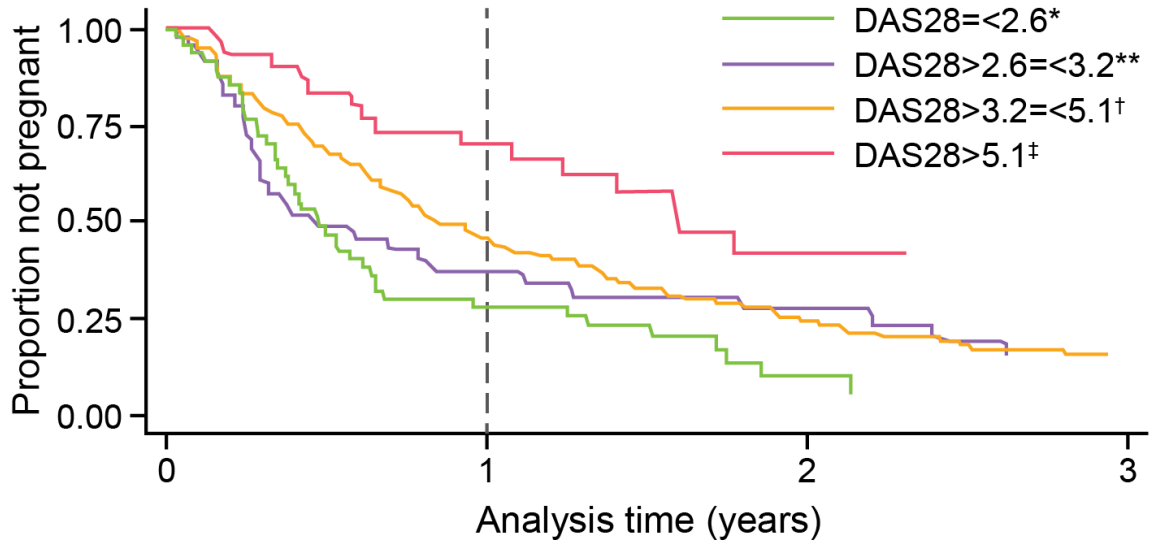
- Options: preference, budget, insurance, faith, culture, lifestyle



33% of patients report ineffective form of birth control[8]

Medications, disease control, and fertility

- Disease activity may affect fertility
- RA patients with high disease activity had a longer time to get pregnant than those with lower disease activity



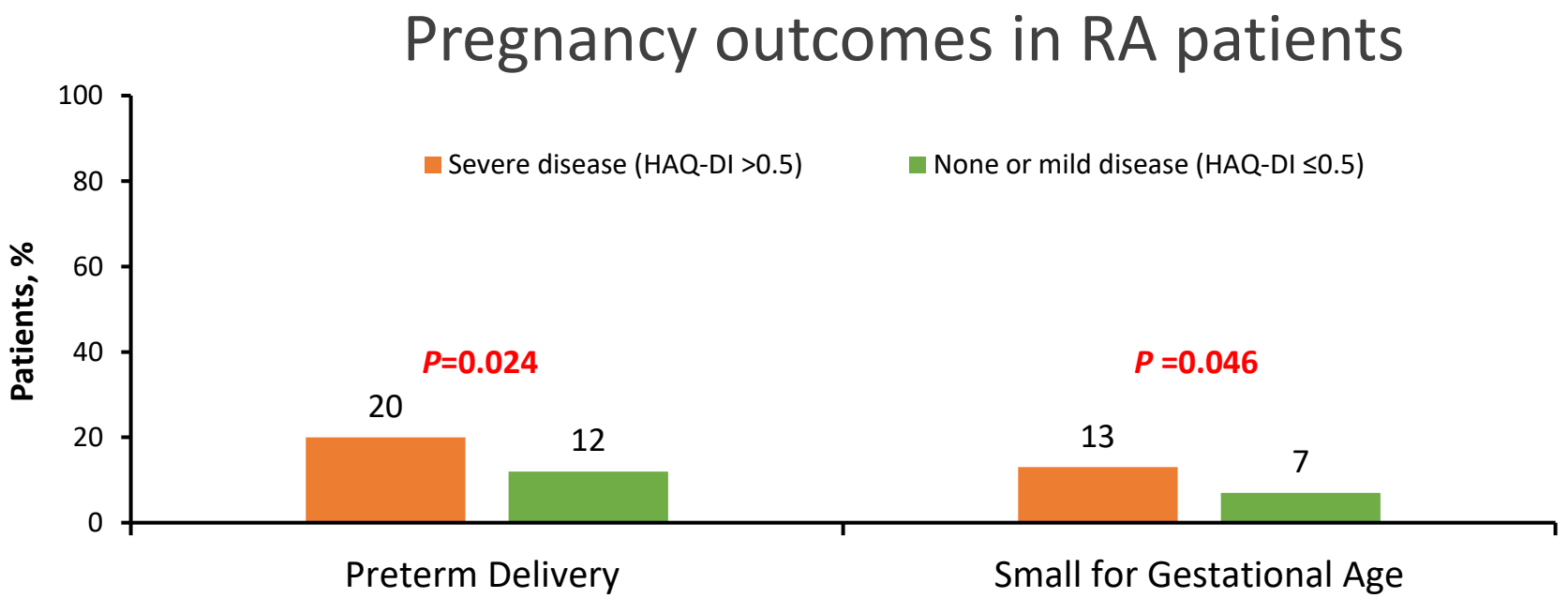
75% of patients with high disease activity during the first year did not achieve pregnancy

Disease activity before pregnancy correlates with disease activity during pregnancy

- In RA, LDA prior to pregnancy predicts LDA during pregnancy[11]
- In PsA and AS, women with LDA or remission prior to pregnancy experienced LDA or remission during pregnancy[12]
- In IBD, ~80% of women in remission prior to pregnancy maintained remission during pregnancy[13]
- In patients with Crohn's disease, 66% of women with active disease prior to pregnancy had active or worsening disease during pregnancy[14]

Low disease activity (LDA) pre-pregnancy is associated with LDA or remission during pregnancy in patients with rheumatic diseases

Uncontrolled disease is associated with negative pregnancy outcomes



Pregnancy outcomes associated with uncontrolled or high disease activity in RA may include preterm delivery, small size for gestational age, and C-section birth[20]

Therefore, achieving low disease activity or remission *prior* to pregnancy in patients with rheumatic diseases is important !!!

Risk of treatment vs. risk of uncontrolled disease

Risks of untreated or under-treated disease leading to poorer pregnancy outcomes

Risks of medication side effects on the mother and the fetus

Treatment options that are safe for pregnancy

Choose a medication that is safe for conception, pregnancy, delivery, post-partum, and breastfeeding

Examples:

- Hydroxychloroquine
- Azathioprine
- TNF-inhibitors
- NSAIDs (until the 3rd trimester, then d/c to prevent premature closure of the ductus arteriosus)
- Steroids

Use shared decision making to empower patients

Shared decision making: A collaborative process between and patient and her provider to make decisions that are guided by evidence and congruent with her value system

Discussion topics:

- Medication options
- Risks, benefits, administration, costs
- Expectations, time of onset
- Adjustments of the plan over time
- Option of no treatment

Ultimately, it's the patient's choice, but…

the provider is obligated to guide her to an informed decision

Concerns about pregnancy…

- Will my disease flare during pregnancy?
- How can I manage morning sickness, fatigue, and work?
- Could the treatments affect my baby?
- Will my baby get my disease?
- Can I breastfeed?
- How many children can I have?
- Will I be able to manage?

Leading fears and concerns of pregnancy in women with rheumatic diseases[15]

10. Miscarriage
9. Ability to get pregnant with diagnosis
8. Disease worsening after pregnancy
7. Having to stop medications during pregnancy
6. Disease worsening during pregnancy
5. Passing disease on to baby
4. Fatigue affecting childcare
3. Pregnant mother's health
2. Health of baby
1. Medications affecting baby

Heritability of Immune-mediated diseases

Patients with autoimmune diseases have an increased risk of having children with the same or other autoimmune diseases:

Disease	Increased risk of child
Rheumatoid arthritis[16]	Up to 8x
Ankylosing spondylitis[17]	16 – 76x
Psoriatic arthritis[18]	31 – 103x
Inflammatory bowel disease[19]	10 – 25x (175x if both parents have IBD)

Patients with autoimmune diseases may choose to have fewer children or no children at all for fear of passing on their disease to their children

Effect of pregnancy on disease activity

Does disease activity get better or worse during pregnancy?

Conventional wisdom: it gets due to increased steroid production

Meta-analysis[21]:

RA: 54% improved; 46% worsening or stable

PsA: 59% improved; 32% worsening; 10% mixed

AS: 40% improved; 60% worsening or stable

Crohn's: 33% remission; 33% stable; 33% worsening

Should you stop medications during pregnancy?

Some providers interrupt therapy during pregnancy, especially biologic treatment in the 3rd trimester.

However:

Treatment discontinuation → Increased risk of flares → Disease aggravation → Poorer outcome

Therefore:

- Choose a medication before pregnancy that a patient can stay on throughout pregnancy
- Achieve LDA or remission before pregnancy to improve outcomes throughout

Does disease flare postpartum?

Conventional wisdom: **YES !!!**

- 90% of patients with AS flare within 1 year postpartum[12]
- 40% of patients with RA flare within 6 months postpartum[11]
- 40% of patients with PsA flare within 1 year postpartum[12]
- 20% of patients with IBD flare within 6 months postpartum[22]

Effects of postpartum flares

Flares may lead to decreased function, pain, and fatigue, impacting

- Holding or carrying child
- Changing child's diaper
- Feeding or nursing child
- Taking care of household and older children
- Maintaining personal health, nutrition, and sleep
- Mood

Stressors can lead to postpartum depression

It takes a village, continued…

Use an interdisciplinary team to provide extended care for the postpartum mother

2020 American College of Rheumatology Guideline for the Management of Reproductive Health in Rheumatic and Musculoskeletal Diseases (RMD)

Purpose: To provide evidence-based recommendations for:

a. Assisted reproductive technologies (ART)
b. Fertility preservation with gonadotoxic therapy
c. Use of menopausal hormone replacement therapy (HRT)
d. Pregnancy assessment and management
e. Medication use in patients with RMD

2020 American College of Rheumatology Guideline for the Management of Reproductive Health in Rheumatic and Musculoskeletal Diseases (RMD)

Methodology:

- Systematic review of 219/11,760 published manuscripts
- Voting panel of rheumatologists, OB/GYNs, reproductive medicine specialists, and patients
- 70% agreement to reach consensus on whether to include or disregard recommendations
- Includes good practice states (i.e. clinical suggestions, like counseling on the use of potentially teratogenic medications)

2020 American College of Rheumatology Guideline for the Management of Reproductive Health in RMD: Recommendations

Contraception:

- Encourage the use of effective long-acting reversible contraception (LARC) for all patients
- Avoid estrogen in antiphospholipid antibody (aPL) positive patients or those with active systemic lupus erythematosus (SLE), using an intra-uterine device or the less-effective progestin-only pill in these patients
- Avoid depot medroxyprogesterone acetate injections in patients at high risk for osteoporosis; and
- Encourage all patients to use over-the-counter morning after emergency contraception, if desired

2020 American College of Rheumatology Guideline for the Management of Reproductive Health in RMD: Recommendations

Fertility/Assisted Reproductive Technology (ART):

- Encourage ART for patients with stable or quiescent disease
- Consider prophylactic anti-coagulation for aPL-positive or obstetric antiphospholipid syndrome (APS) patients
- Continue immunosuppressants, other than cyclophosphamide (CYC), for oocyte retrieval for cryopreservation or surrogacy
- Do not automatically use prophylactic prednisone in SLE patients; treat with prednisone if a flare develops
- Consider co-therapy with a gonadotropin-releasing hormone analog for women on IV CYC

2020 American College of Rheumatology Guideline for the Management of Reproductive Health in RMD: Recommendations

Menopause

- Consider hormone-replacement therapy (HRT) in aPL-negative women with SLE. Use the lowest dose to alleviate symptoms for the minimum time necessary immediately following menopause onset
- Avoid HRT in aPL-positive women
- Consider transdermal over oral HRT to reduce venous thromboembolism risk

2020 American College of Rheumatology Guideline for the Management of Reproductive Health in RMD: Recommendations

Pregnancy Assessment and Management

- In patients taking medications not compatible with pregnancy, switch to a pregnancy-compatible medication, observe for a time, and assess for tolerability and efficacy of the new drug before attempting pregnancy
- Start a pregnancy-compatible medication if active disease develops during pregnancy
- Check anti-Ro/SSA, anti-La/SSB, and aPL antibodies before or early in pregnancy
- Continue hydroxychloroquine
- Consider low-dose aspirin to prevent preeclampsia, and start this in the first trimester
- In women with SSc, start ACE-inhibitor if patient develops scleroderma renal crisis

2020 American College of Rheumatology Guideline for the Management of Reproductive Health in RMD: Recommendations

Medication use for men:

- Discontinue CYC 12 weeks before and thalidomide 4 weeks before attempting to conceive
- Continue hydroxychloroquine, colchicine, azathioprine, TNF inhibitors, sulfasalazine, methotrexate, leflunomide, mycophenolate, cyclosporine, tacrolimus, anakinra, and rituximab
- Consider semen analysis if a couple has trouble conceiving while the man is on sulfasalazine

2020 American College of Rheumatology Guideline for the Management of Reproductive Health in RMD: Recommendations

Medication use for women:

- Discontinue CYC, thalidomide, mycophenolate, methotrexate, and leflunomide with a wash-out of leflunomide before pregnancy and immediately if pregnant
- Consider stopping NSAIDs if a woman has difficulty conceiving; don't use in the 3rd trimester
- Continue hydroxychloroquine, sulfasalazine, colchicine, and azathioprine during pregnancy; continue TNF inhibitors if clinically necessary
- Consider CYC in the 2nd or 3rd trimester or rituximab during pregnancy in women with organ- or life-threatening disease
- Continue low-dose steroids in women on non-fluorinated steroid therapy, if needed

2020 American College of Rheumatology Guideline for the Management of Reproductive Health in RMD: Recommendations

Breastfeeding

- Female patients should be encouraged to breastfeed if they desire and to maintain disease control with medications compatible with lactation
- While breastfeeding, women should avoid CYC, thalidomide, mycophenolate, leflunomide, and methotrexate
- While breastfeeding, women should continue hydroxychloroquine, TNF inhibitors, rituximab, and non-fluorinated steroids
- Women on steroids >20 mg/day should avoid breastfeeding within 4 hours of taking their drug and discard any milk pumped or expressed in that same window

Conclusions

- Pregnancy and women's health in the rheumatic diseases requires a coordinated and interdisciplinary approach
- A woman's reproductive journey begins at menarche and ends at menopause; it can be a carousel with multiple touchpoints
- Optimize care during family planning, pregnancy, breastfeeding, and the postpartum period for your female patients
- The 2020 American College of Rheumatology Guidelines for the Management of Reproductive Health in RMD provide evidence-based recommendations for ART, fertility preservation, HRT, pregnancy assessment and management, and medication use.

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