AMERICAN COLLEGE of RHEUMATOLOGY
Empowering Rheumatology Professionals

Navigating Reproductive Health in Patients with Systemic Lupus Erythematosus (SLE)

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Its contents are solely the responsibility of the authors and do not necessarily reflect the official views of GlaxoSmithKline.

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Disclosures:

Conflict of Interests of the Authors

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    - *All relevant financial relationships have been mitigated*.

Learning Objectives

At the end of this presentation, learners will be able to:

- Appreciate the impact of pregnancy on SLE disease activity and the risk of adverse pregnancy outcomes in women with SLE
- Recognize the importance of pre-conception counseling
- Identify disease specific management for pregnant SLE patients including the safety of common SLE meds in pregnancy and lactation

Systemic Lupus Erythematosus

- Multisystem disease affecting many organ systems
- Occurs in reproductive aged woman
- More common and more severe in Black or African-American, Hispanic and Asian populations
- Active disease can lead to poor pregnancy outcomes

SLE and Family Planning

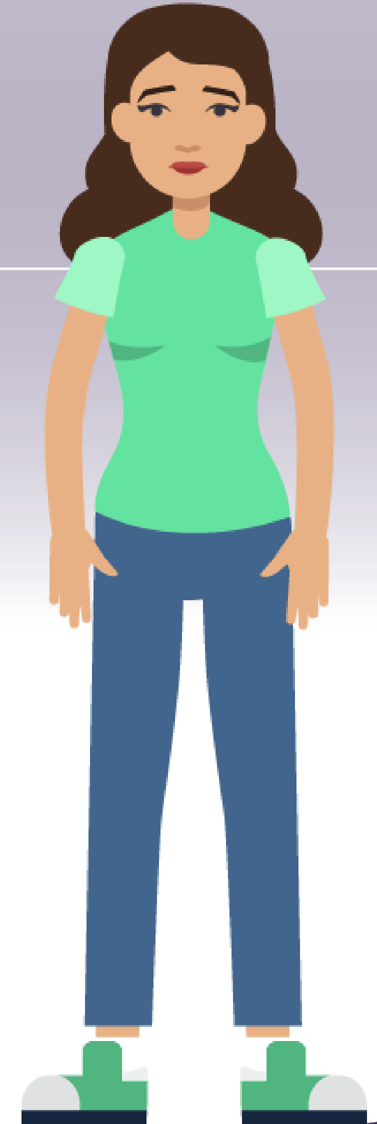
Basic premises:

- When discussing family planning with patients, one must be respectful of differences in individual's attitudes that often reflect cultural, religious, and personal values
- As SLE disproportionally affects racial and ethnic minorities, one must be mindful of existing healthcare disparities when discussing management options
- Providers should self-reflect on their unconscious biases when discussing family planning with patients

Lupus in Pregnancy

Let's Start with a Case

- Clara is an 18 y.o. female with history of SLE and Lupus Nephritis (LN) class III seen in routine follow up for primary care
- She is taking hydroxychloroquine (HCQ) and prednisone 2.5mg. Formerly on mycophenolate but weaned off of this medication 3 years ago
- Recently developed arthritis and she was started on methotrexate



At her visit, what is the one key question to address at this encounter regarding her reproductive health?

Would you like to become pregnant in the next year?

She answers….

- Clara replies she would not like to become pregnant within the year, but may become sexually active
- You counsel her regarding contraception and pregnancy avoidance given that methotrexate is teratogenic and abortigenic

What lab data do you need to help aid your discussion of contraception?

Her antiphospholipid antibody panel (aPL)

- Anti-Cardiolipin IgG/IgM
- Anti-Beta-2-glycoprotein IgG/IgM
- Lupus anticoagulant also called DRVVT

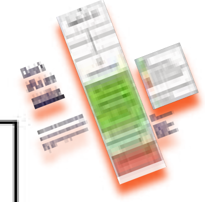
Assess aPL status

Positive aPL test

IUDs* (preferred) or progestin-only pill (less effective) [4]

AVOID combined estrogen-progestin contraceptives [3]

Negative aPL test



Non-SLE RMD

IUDs*, progestin implant, combined estrogen and progesterone pill, progestin-only pill (less effective), transdermal patch, vaginal ring, or DMPA [1]

IUDs or progestin implant preferred over other hormonal contraceptives [1A]

SLE Low disease activity

IUDs*, progestin implant, combined estrogen and progesterone pill, progestin-only pill (less effective), vaginal ring, or DMPA [2]

IUDs or progestin implant preferred over other hormonal contraceptives[2A]

AVOID estrogen patch [2B]

SLE Mod-high disease activity

IUDs*, progestin implant, DMPA, or progestin-only pill over combined estrogen-progestin contraceptives [2C]

AVOID estrogen patch [2B]

SPECIAL CIRCUMSTANCES:
Use of mycophenolate medications requires an IUD or the combination of two other forms of contraception [11].

Avoid DMPA in patients at risk for osteoporosis [10]

LEGEND

- Strongly recommend
- Conditionally recommend
- Conditionally recommend against
- Strongly recommend against

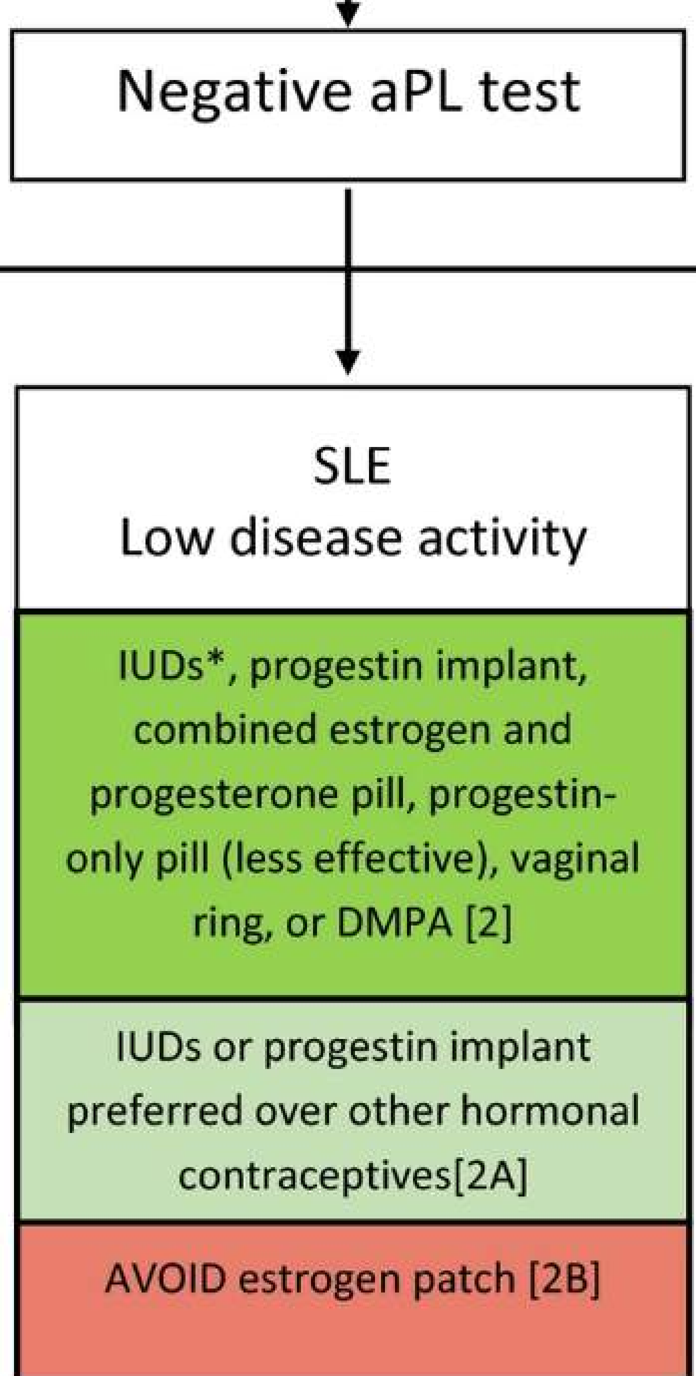
Bracketed #'s refer to Recommendation # (See Appendix 7)

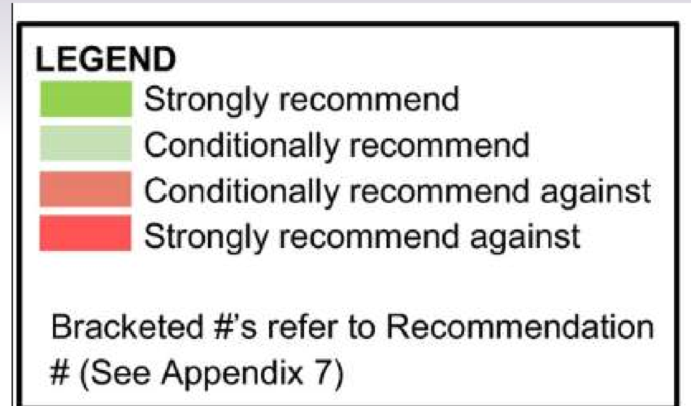
* Recommendation for IUD use includes women receiving immunosuppression therapy [7]

Source:
2020 ACR Guideline for the Management of Reproductive Health in Rheumatic and Musculoskeletal Diseases

Clara's aPLs are <u>negative</u>

IUD=Intrauterine device (hormonal or copper)
RMD= Rheumatic and musculoskeletal disease
DMPA= Depot medroxyprogesterone acetate "Depo" shot





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Assess aPL status

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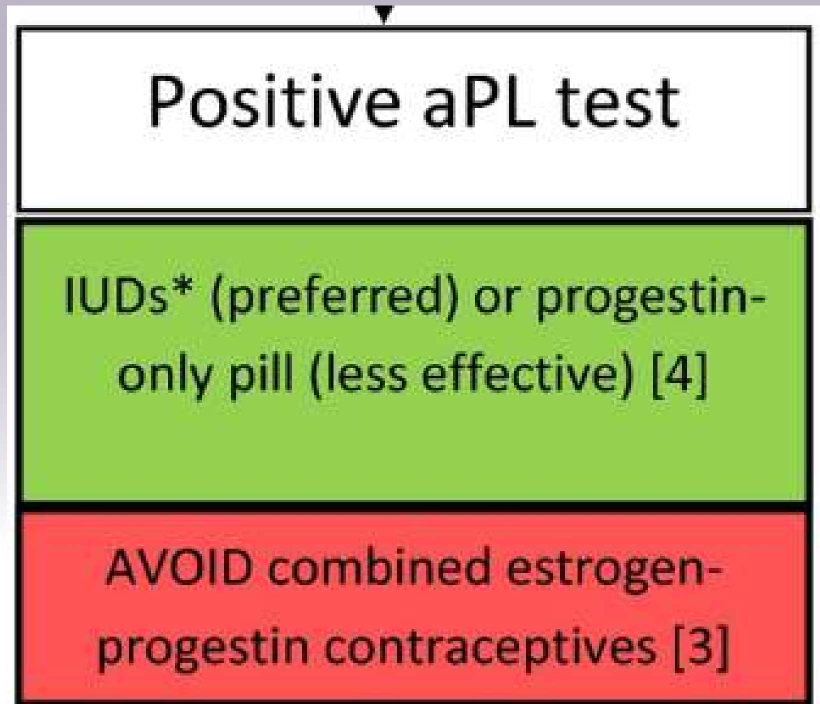
What if she had <u>positive</u> aPLs?



If aPLs results are equivocal, refer to specialist

LEGEND
Strongly recommend
Conditionally recommend
Conditionally recommend against
Strongly recommend against

Bracketed #'s refer to Recommendation # (See Appendix 7)

IUD=Intrauterine device (hormonal or copper)
RMD= Rheumatic and musculoskeletal disease
DMPA= Depot medroxyprogesterone acetate "Depo" shot

Source:
2020 ACR Guideline for the Management of Reproductive Health in Rheumatic and Musculoskeletal Diseases

Next steps……

- aPL laboratory evaluation returns negative
- Clara decides she would like to try the Depot medroxyprogesterone acetate shots (DMPA) and you arrange for her to receive her first one in clinic
- You also recommend barrier contraception to help prevent sexually transmitted diseases

Two years pass……

- She has not been following up with providers and has not been taking her SLE medications or DMPA for at least 1 year
- She has a positive pregnancy test at home
- She contacts her primary care provider's office

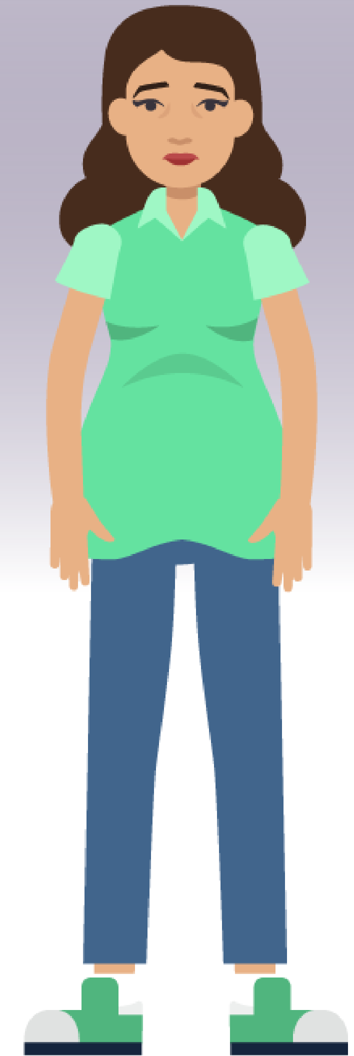
Importance of planning lupus pregnancies

When lupus pregnancies are un-planned, there are risks of:

- High lupus activity at the time of conception
- Exposing the fetus to medications that are not compatible with pregnancy
- Inappropriate discontinuation of indicated pregnancy-compatible medications
- Increased adverse pregnancy outcomes
- Increased adverse neonatal outcomes

What if she had been taking her methotrexate when she became pregnant?

- Stop methotrexate
- Refer to Maternal Fetal Medicine (MFM) specialist
- Refer to https://mothertobaby.org/ for reporting of exposure



Drug Safety Overview: Pregnancy

Pregnancy Compatible
Azathioprine
Chloroquine
Colchicine
Cyclosporine
Hydroxychloroquine
NSAIDs *[discontinue at 20 weeks]*
Prednisone *(<20 mg/day)*
Sulfasalazine
Tacrolimus

NOT Compatible with Pregnancy	Notes
Belimumab	*Discuss discontinuation at conception*
Cyclophosphamide	*Consider if life/organ threatening disease in 2nd or 3rd trimester*
Leflunomide	*Use cholestyramine washout until level is undetectable*
Methotrexate	*Stop 1 – 3 months before trying to conceive*
Mycophenolate mofetil; Mycophenolic acid	*Discontinue 6 weeks before trying to conceive*
Rituximab	*Can be continued until conception; Consider if life/organ threatening disease in 2nd or 3rd trimester*
Thalidomide Lenalidomide	*Stop 1 month before trying to conceive*

Next steps in her pregnancy……

- Review Clara's medication list for safety in pregnancy
- Re-start her HCQ
- Verify not taking methotrexate
- Prescribe a prenatal vitamin
- Obtain basic lab work: CBC with differential, CMP, Urinalysis
- Refer her to rheumatology

Pregnancy course……

- Clara misses multiple scheduled visits
- She presents at 32 weeks to her obstetrician with headaches and leg swelling and 10 pounds weight gain in the last week.
  - Her blood pressure is 140/90
  - Urinalysis shows 3+ protein and 1+ blood
- Her OB is wondering if this is pre-eclampsia or lupus nephritis

Lupus Nephritis or Pre-eclampsia?

Overlapping features

- Edema
- Hypertension
- Headache/Mental status changes
- Proteinuria
- Increasing creatinine
- Thrombocytopenia

If you are concerned about any of these, be sure to involve: Rheumatology, Nephrology and Maternal Fetal Medicine

The hospital she is referred to should also have a Neonatal Intensive Care Unit (NICU)

Hospital Course……

- Clara is hospitalized for further work-up of possible lupus nephritis versus pre-eclampsia

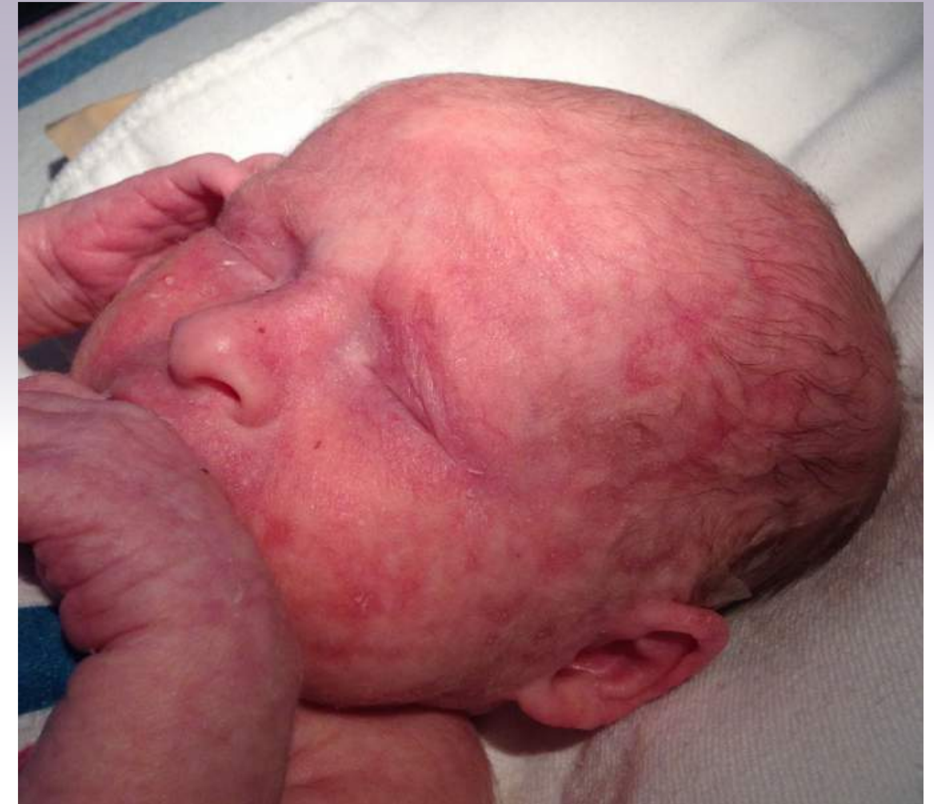
- Multi-disciplinary care team of Nephrology, Rheumatology, and OBGYN, MFM, Neonatology weigh in

Hospital Course......

- Clara is given corticosteroids to promote fetal lung maturation and undergoes emergency c-section delivery due to concerns about pre-eclampsia
- Clara delivers a small, preterm female infant who is admitted to the NICU
- Clara does well and is discharged after 48 hours

Meanwhile the baby……

- Clara's baby remains in the NICU for several weeks as she is weaned from oxygen. Her growth is monitored and feeding tube eventually removed
- Clara's baby is eventually transferred to a step-down unit where she is placed near a window
- The neonatologist caring for the baby observes a new skin finding



A new rash appears ……

Importance of screening for SSA and SSB antibodies:

- Clara did not undergo preconception counseling, SSA/Ro and SSB/La were never checked
- These antibodies should be checked in all women with autoimmune conditions prior to or during pregnancy to help counsel on the risks of neonatal lupus, Clara's were found to be positive after she delivered
- Women with SSA/Ro and/or SSB/La antibodies should undergo serial fetal neonatal cardiac monitoring during pregnancy to screen for fetal heart block
- Hydroxychloroquine may help prevent heart block and is a safe medication in pregnancy

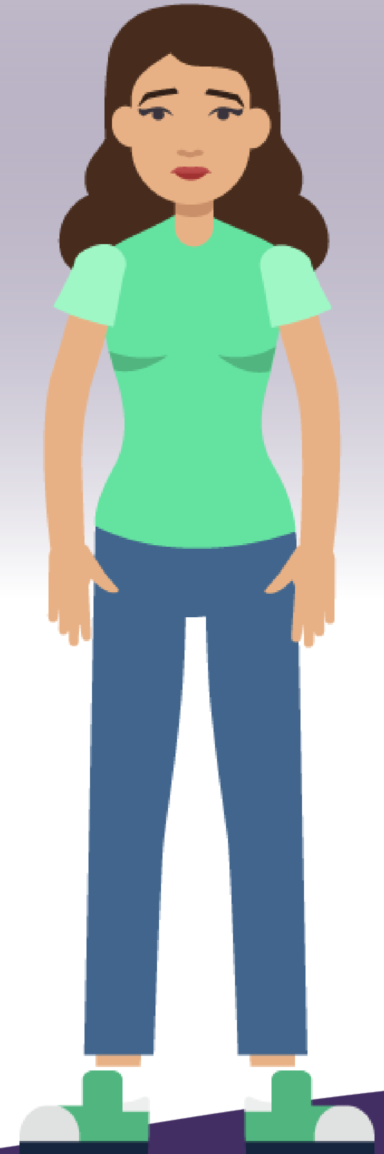
Post-Partum course……

- Clara is found to have SSA/Ro antibodies
- Her baby is diagnosed with neonatal lupus
- Baby’s EKG and Echocardiogram are unremarkable
- Her baby is discharged home almost 2 months in the NICU
- The rash resolves at 6 mont

Post-Partum course……

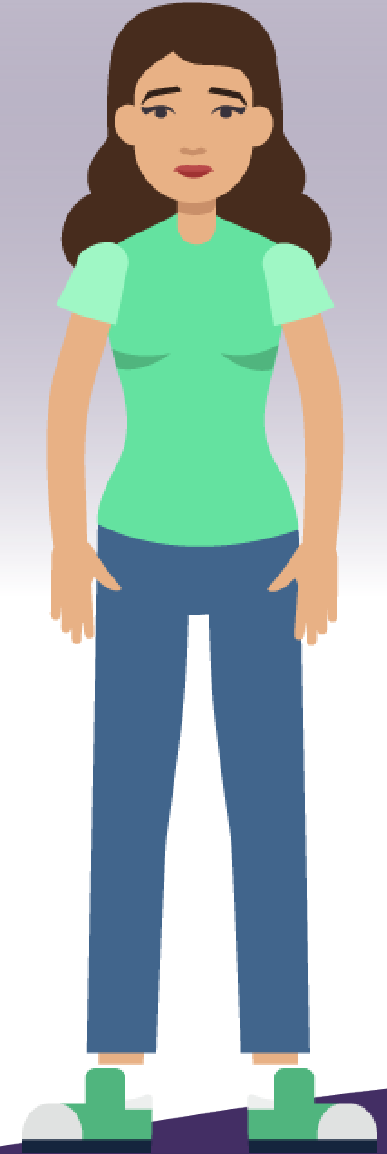
- Clara restarts DMPA "Depo" shot for contraception post-partum

- Clara establishes care with a rheumatologist



Several years later…….

- Clara decides she **would like to have another child.** She is on DMPA for birth control.
- Lupus has been in **remission for the past year**
- Current **medications include**
  - Hydroxychloroquine (HCQ)
  - Prednisone 2.5mg
  - Mycophenolate mofetil



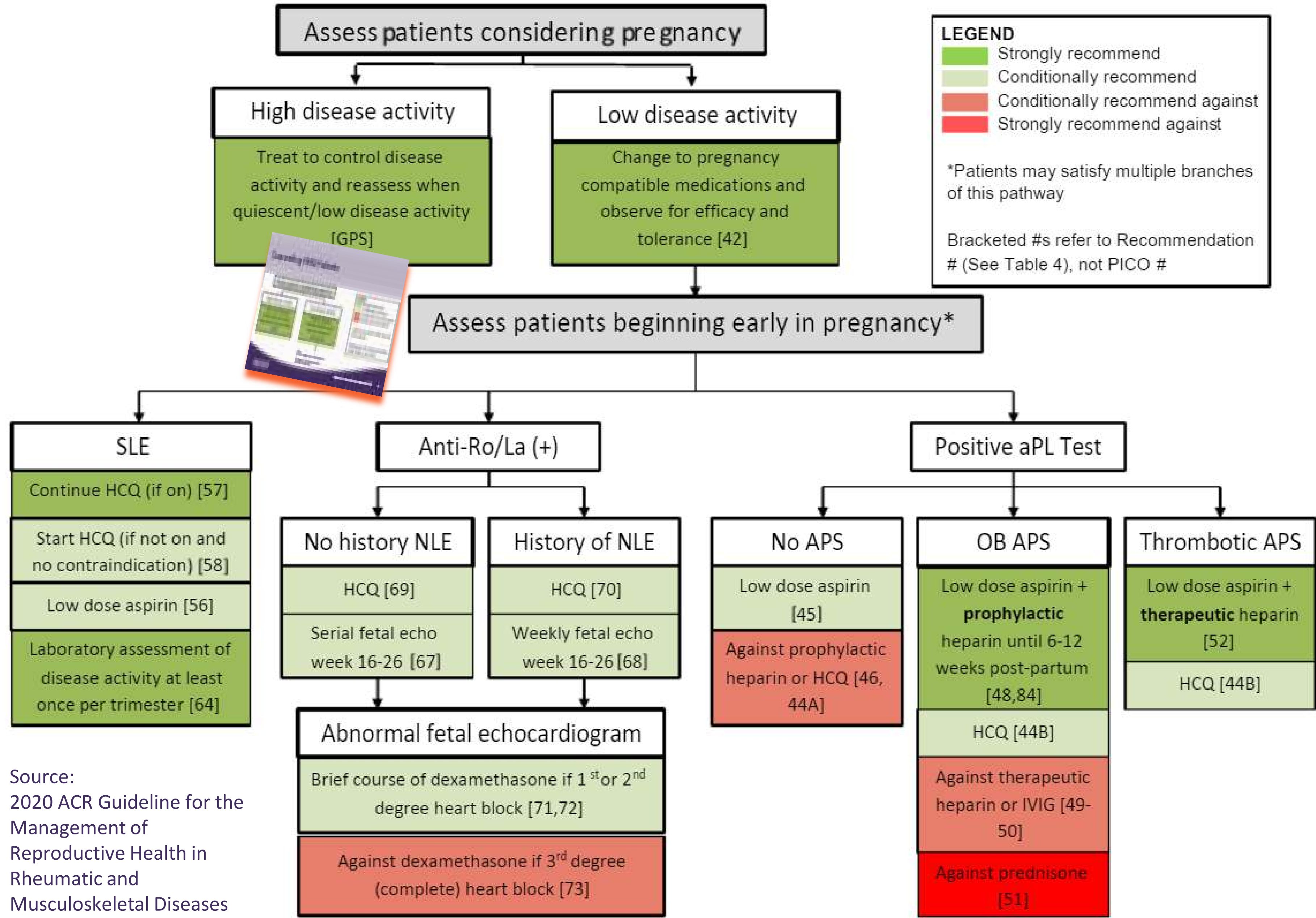
What are some initial important topics to address during your pre-conception counseling?

- **Improved maternal and pregnancy outcomes** when disease activity is low at least 6 months prior to conception

- **Medication** compatibility with pregnancy

- Factors that increase **pregnancy and fetal risks**

Counseling Rheumatic Disease (RMD) Patients



Source:
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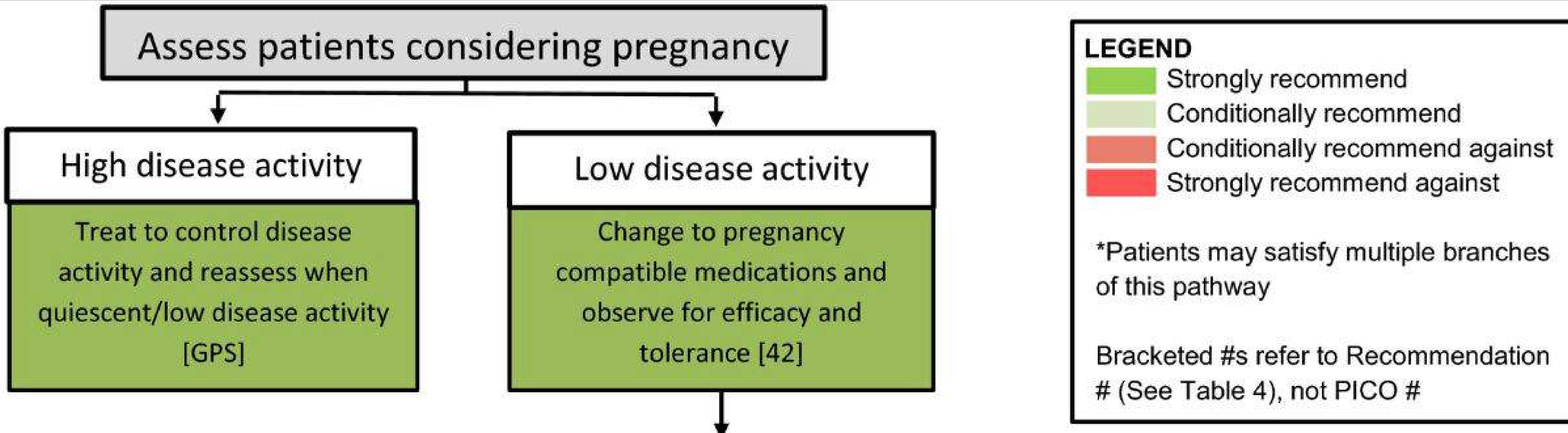
Counseling RMD Patients



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Next step in Pre-conception Counseling……

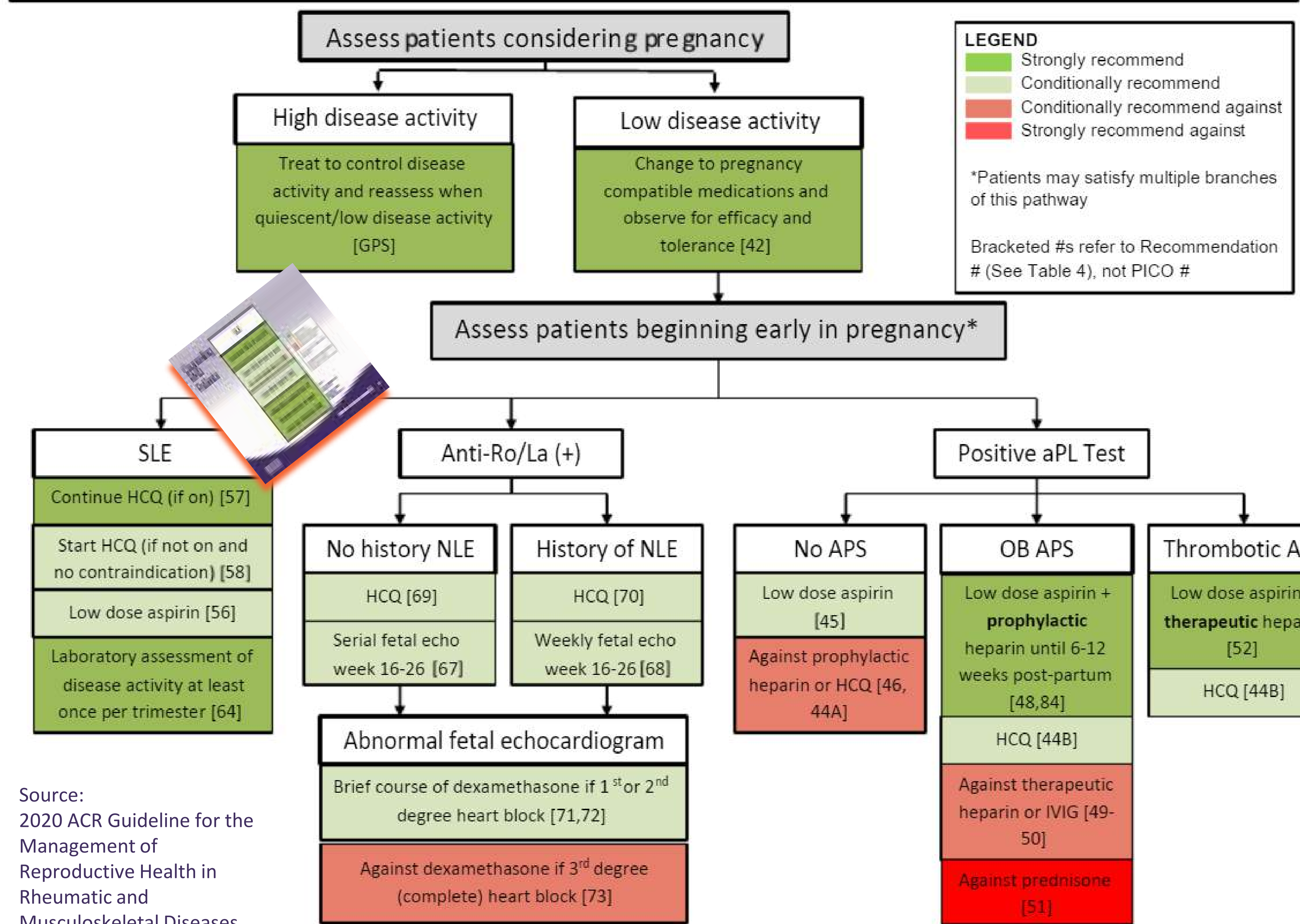
- You review Clara's recent labs from her rheumatologist. They reveal normal kidney function, quiescent disease activity and normal urine studies.
- What if Clara had evidence of kidney damage*?*
    - Refer to a Nephrologist and MFM
- If a lupus patient has significant organ related damage, refer for consultation to specific organ related specialist before conception

Pre-conception Medical Management

Transition patients to pregnancy compatible medications and observe for several months prior to conception

- For example, a patient on mycophenolate mofetil should be transitioned to azathioprine and/or tacrolimus and observed for several months before trying to conceive

Counseling RMD Patients



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Counseling RMD Patients

SLE
Continue HCQ (if on) [57]
Start HCQ (if not on and no contraindication) [58]
Low dose aspirin [56]
Laboratory assessment of disease activity at least once per trimester [64]

LEGEND
- Strongly recommend
- Conditionally recommend
- Conditionally recommend against
- Strongly recommend against

*Patients may satisfy multiple branches of this pathway

Bracketed #s refer to Recommendation # (See Table 4), not PICO #

Source:
2020 ACR Guideline for the Management of Reproductive Health in Rheumatic and Musculoskeletal Diseases

Importance of Hydroxychloroquine (HCQ)

- All pregnant SLE patients should remain on hydroxychloroquine unless contra-indicated
- Improves maternal outcomes
- Improves infant outcomes

Importance of Low Dose Aspirin (81 or 100mg)

- Pre-eclampsia risk is increased in women with SLE, particularly Black or African American women with SLE
- All pregnant women with SLE recommended to take daily low dose aspirin to lower preeclampsia risk
- Start at 12-16 weeks gestation
- Continue until delivery

Next step in Pre-conception Counseling

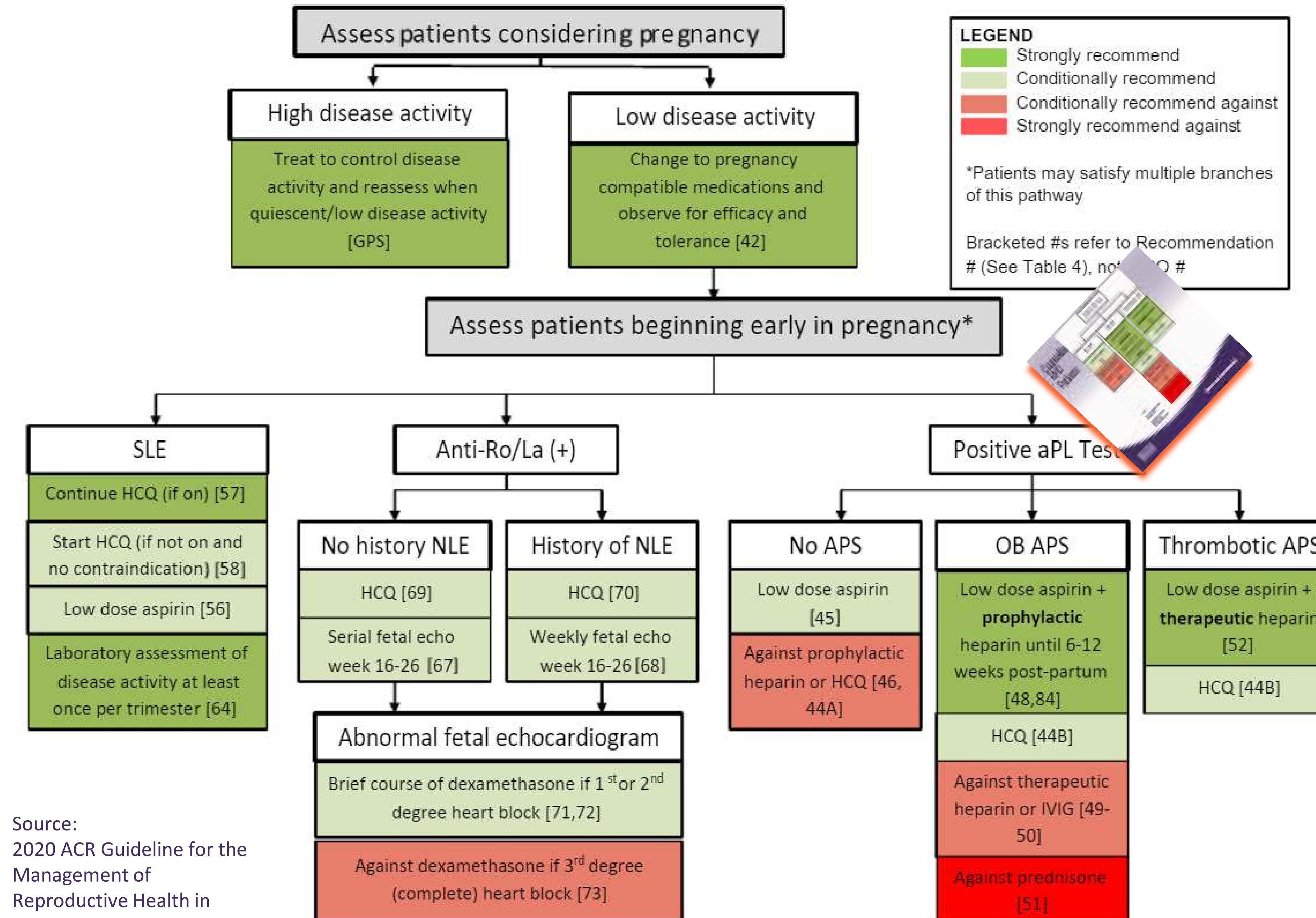
If you didn't have Clara's prior records, what additional labs would help to evaluate her pregnancy risks?

Antiphospholipid antibodies (aPLs)

- Anti-Cardiolipin IgG/IgM
- Anti-Beta-2-glycoprotein IgG/IgM
- Lupus anticoagulant also called DRVVT
- Anti-SSA/Ro and SSB/La

Counseling RMD Patients

- We know that Clara's aPL test was negative.
- However, if Clara's aPL test came back positive, what would you do?



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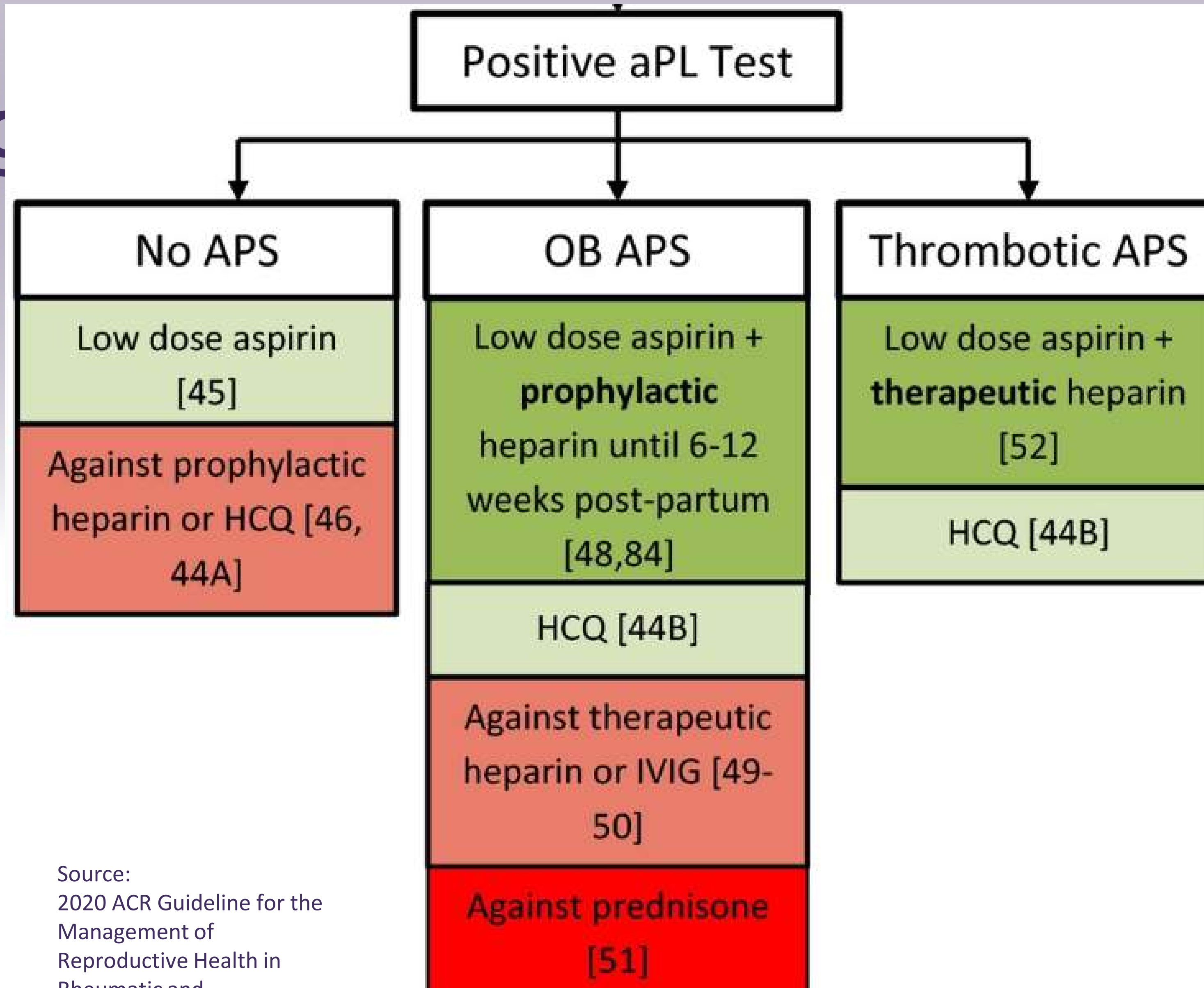
Counseling RMD Patients



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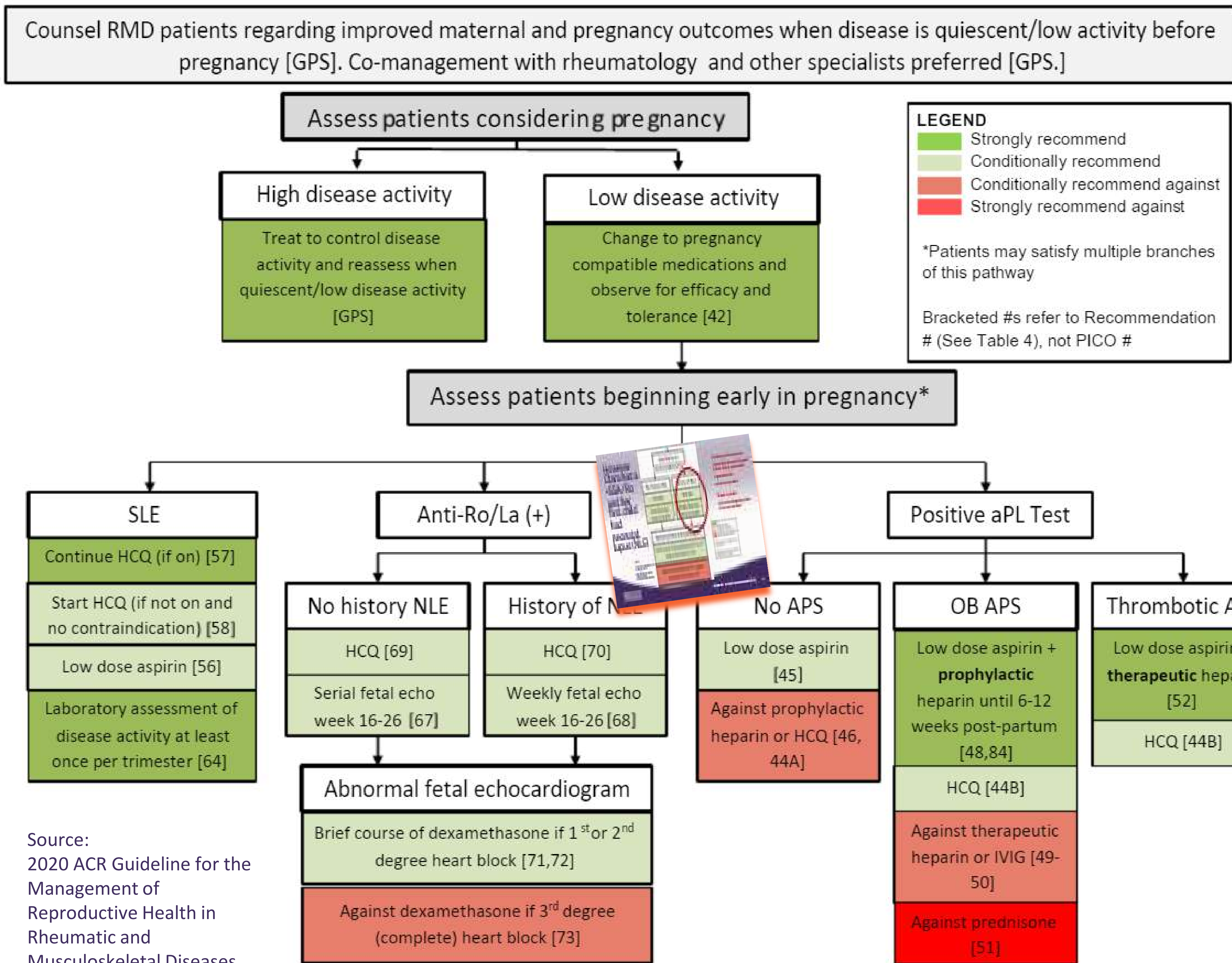
Counseling RMD Patients

- Next, let's look at Anti-Ro/La
- We know that Clara's first baby had neonatal lupus (NLE)



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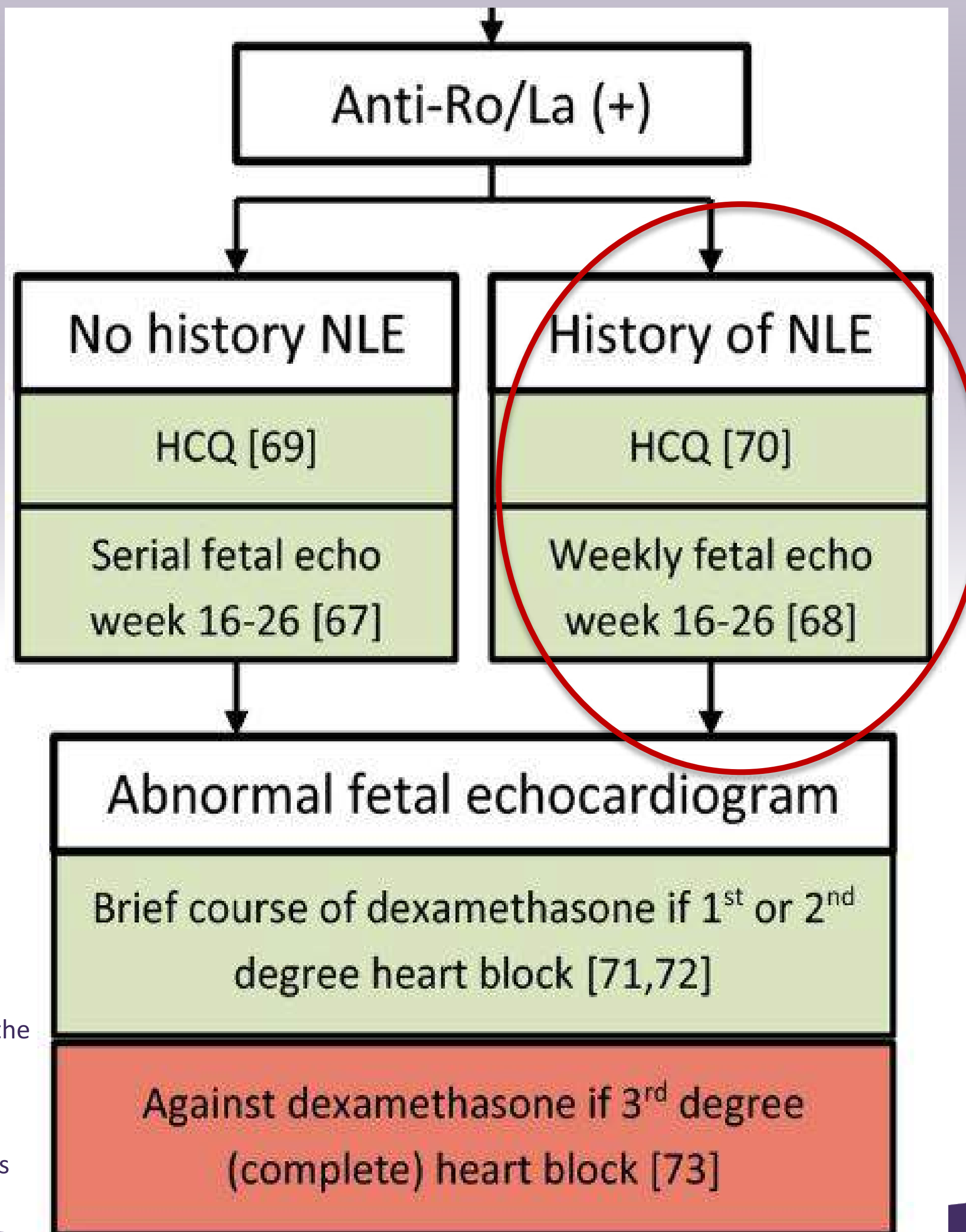
However Clara has a +SSA/Ro and her first child had neonatal lupus (NLE)



Source:
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Hydroxychloroquine may help prevent heart block from neonatal lupus and is recommended

Weekly fetal echocardiograms are recommended

LEGEND
- Strongly recommend
- Conditionally recommend
- Conditionally recommend against
- Strongly recommend against

*Patients may satisfy multiple branches of this pathway

Bracketed #s refer to Recommendation # (See Table 4), not PICO #

Your Pre-conception Recommendations for Clara

- You recognize mycophenolate is not compatible with pregnancy
- You suggest she talk to her rheumatologist about her desires to become pregnant
  - You reassure her that hydroxychloroquine and low dose prednisone are compatible with pregnancy
  - You recommend she start ASA 81 mg daily at 12-16 weeks gestation for pre-eclampsia risk reduction

Clara meets with her rheumatologist who....

- Stops her mycophenolate and starts azathioprine
- After 5 months on this new medication, her lupus remains inactive and together she and her doctor agree it is a good time to try to conceive
- Then stops her DMPA
- Since she has a +SSA/Ro and a child with neonatal lupus, she will need fetal cardiac monitoring in the second trimester during future pregnancies

Clara comes to clinic and is Pregnant for the Second Time……

- She tells you she is “achy” and fatigued; she doesn’t know if this is “her Lupus acting up” or just the signs of her pregnancy
- You review she is taking azathioprine, HCQ, low dose prednisone
- Her SLE disease activity should be monitored at least once per trimester with clinical history, examination, and laboratory tests
- You recommend she continues to follow up with her rheumatologist

Vaccines in Pregnancy

- Pneumococcal , influenza (“flu”), Tdap, and hepatitis B vaccines are recommended when indicated
- COVID-19 vaccine is recommended in pregnant women and those with rheumatic diseases
- MMR vaccines should not be administered to pregnant women

2nd Trimester……

- At 14 weeks, she starts aspirin 81mg daily
- At 18 weeks, she begins routine fetal echocardiograms
- She regularly sees OBGYN, MFM, and Rheumatology
- She has no signs of active lupus or pre-eclampsia
- Clara continues on azathioprine, prednisone 2.5mg, and hydroxychloroquine throughout her pregnancy

Clara tells you she would like to breastfeed and is wondering about the safety of her current medications.

Drug Safety Overview: Breastfeeding

Compatible with Breastfeeding
Azathioprine *[low transfer]*
Belimumab *[expect minimal transfer but no available data]*
Colchicine
Cyclosporine *[low transfer]*
Hydroxychloroquine/Chloroquine
NSAIDs *[Ibuprofen preferred]*
Prednisone *(delay 4 hours after a dose of >20 mg/day)*
Rituximab
Sulfasalazine
Tacrolimus *[low transfer]*

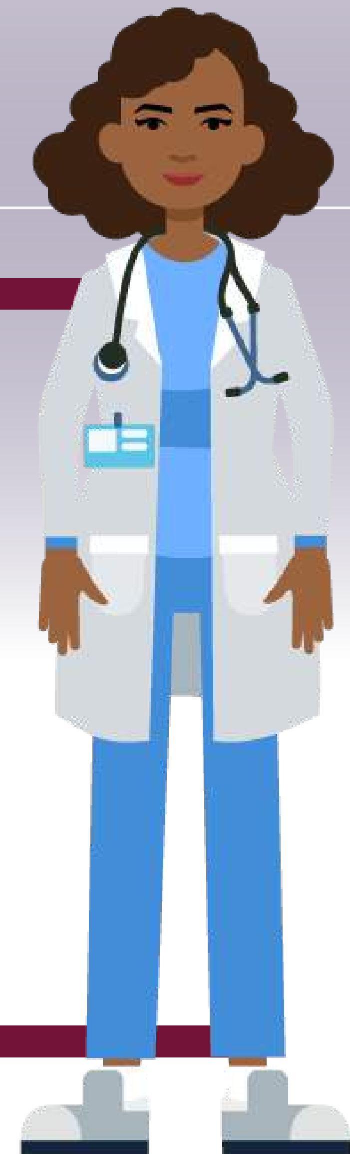
NOT Compatible with Breastfeeding
Cyclophosphamide
Leflunomide
Methotrexate
Mycophenolate mofetil
Mycophenolic acid
Thalidomide

Clara delivers a healthy baby girl at 39 weeks

- Her lupus remained quiescent and she did not have signs of pre-eclampsia
- She and her baby are discharged home after 48 hours
- She continues post-partum on azathioprine, prednisone 2.5mg, and hydroxychloroquine, all medications compatible with breastfeeding

Key Learning Points

- Drug safety
- Importance of HCQ and baby ASA
- When to refer



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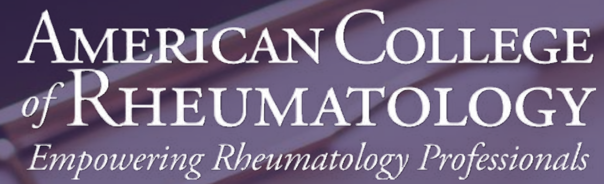

Thank You

Let us know what you learned!
Please remember to take your post-test!

Collaborative Initiatives (COIN)
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https://acrreprohealthinitiative.com/