Guidelines about Systemic Lupus Erythematosus (SLE) and Pregnancy

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Questions - Points of discussion

• As a patient with lupus, can I ever have a baby?

• What should I know before I get pregnant?

• What steps do I need to take to ensure a safe pregnancy for me and my baby?

• How can lupus and lupus medications affect my chances of getting pregnant and my pregnancy outcome?

• Which lupus medications are safe and which ones are contraindicated in pregnancy?

• During pregnancy, do I need to be monitored differently than women without lupus?

• How can lupus affect my pregnancy and how can pregnancy affect my lupus?
General principles

- Changing mentality:
  - Caution against pregnancy → Embracing pregnancy

- Early discussion of family planning

- Support of lupus patient and her family in their family planning decisions

- Individualized risk assessment

- Pre-conception counseling

- Preventive strategies and monitoring before and during pregnancy
Fertility and SLE

• Lupus *does not* reduce fertility *per se*

*What does?*

• **Active** lupus and especially active kidney lupus (nephritis)
• Certain lupus medications might ↓ fertility
  – Cyclophosphamide (Cytoxan)
    • Age and dose- related effect
    • Pre-treatment with certain medications (Lupron) may decrease risk
• Alcohol
• Smoking
Pregnancy planning in SLE

• Discuss your plans with your Rheumatologist **early**

• Risk assessment
  – Lupus disease activity
  – Lupus nephritis
  – Chronic kidney insufficiency
  – Other medical conditions
  – Review of previous pregnancies (miscarriages, preterm births, complications)
  – Current medications: safe for the baby? Need to be changed? Can they be changed?
    – anti-Ro/SSA or anti-La/SSB positive
    – Anti-phospholipid antibodies (APS)

*BEFORE you get pregnant*
Pre-conception Evaluation

- Assess major organ function: Advise against pregnancy if severe dysfunction (Table 1)
- Assess disease activity:
  - Stable - Proceed
  - Active - Defer pregnancy
- Obtain autoantibody profile for risk evaluation, especially aPL and anti-Ro antibodies
- Review medications and adjust to achieve optimal control on safe drugs before conception
Potential pregnancy complications in lupus (I)

For mother:
- Pre-eclampsia/ Eclampsia
- HELLP syndrome
- Blood clots
- Lupus flare

For baby:
- Pre-term babies
- Small for age
- Developmental problems
- Pregnancy loss/ miscarriage

(Regional blood pressure, protein in urine, kidney, liver and blood count changes)
Potential pregnancy complications in lupus (II)

• Neonatal lupus
  • Skin, blood counts, heart, liver
  • Transient

• Heart problems (baby)
  • Can be severe
  • May require pacemaker at birth
**Disease-related risk factors**

- SLE activity/flares* (in the last 6–12 months or at conception)
- Lupus nephritis (history or active at conception†)
- Serological (serum C3/C4, anti-dsDNA titres) activity
- Previous adverse pregnancy outcome(s)
- History of vascular thrombosis
- SLE diagnosis
- aPL profile‡

**Anti-Ro/SSA, anti-La/SSB antibodies**

**End-stage organ damage and associated comorbidities**

General risk factors

- Maternal age
- Arterial hypertension
- Diabetes mellitus
- Overweight/obesity
- Thyroid disease
- Nicotine and alcohol use

# SLE-related risk factors

<table>
<thead>
<tr>
<th>Disease-related risk factors</th>
<th>Prognostic implications</th>
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</table>
| SLE activity/flare(s) (*) (in the last 6–12 months or at conception)                        | Increased risk for (i) maternal disease activity (RR 2.1 for subsequent flare during pregnancy and puerperium);  
(ii) hypertensive complications (OR 1.8 for PE);  
(iii) fetal morbidity and mortality (OR 5.7 for pregnancy loss, 3.5 for IUGR) |
| Lupus nephritis (history or active at conception†)                                         | Strong predictor of poor maternal (RR 9.0 for renal flare during/after pregnancy)  
and fetal outcome(s) (OR 7.3 for fetal loss and 18.9 for preterm delivery) |
| Serological (serum C3/C4, anti-dsDNA titre) activity                                       | Increased risk for maternal SLE flares during pregnancy (OR 5.3)  
and pregnancy loss                                                                 |
| Previous adverse pregnancy outcome(s)                                                      | APS: increased risk for pregnancy complications                                          |
| History of vascular thrombosis                                                            | APS: increased risk (ORs ranging 3.6–12.7) for pregnancy morbidity                      |
| SLE diagnosis                                                                              | APS: increased risk (OR 6.9) for pregnancy morbidity                                     |
| aPL profile†                                                                               | SLE: strong predictor of adverse maternal and fetal outcomes, especially for patients with persistent moderate-to-high aPL titres, LA and multiple aPL positivity (high-risk aPL profile)  
APS: high-risk aPL profile correlates with increased risk of maternal vascular thrombotic events during pregnancy (OR 12.1),  
(pre-) eclampsia (OR 2.3)  
APS-related pregnancy morbidity (OR 9.2)  
IUGR (OR 4.7)  
preterm birth |
| Anti-Ro/SSA, anti-La/SSB antibodies                                                        | Linked to development of neonatal lupus, including a low risk (0.7–2%) for CHB (especially if moderate-to-high anti-Ro titre(s)),  
weak association with other pregnancy complications |
| End-stage organ damage and associated comorbidities                                         |                                                                                         |

Table 1

Situations where pregnancy is not advisable in patient with SLE

<table>
<thead>
<tr>
<th>Contra-indications to pregnancy:</th>
</tr>
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<tbody>
<tr>
<td>Severe pulmonary hypertension (systolic pulmonary artery pressure &gt; 50mm Hg)</td>
</tr>
<tr>
<td>Severe restrictive lung disease (Forced vital capacity &lt; 1 L)</td>
</tr>
<tr>
<td>Advanced renal insufficiency (creatinine &gt;2.8 mg/dL)</td>
</tr>
<tr>
<td>Advance heart failure</td>
</tr>
<tr>
<td>Previous severe preeclampsia or HELLP despite therapy</td>
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**Pregnancy should be deferred:**

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<tbody>
<tr>
<td>Severe disease flare within last 6 months</td>
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<tr>
<td>Active lupus nephritis</td>
</tr>
<tr>
<td>Stroke within the previous 6 months</td>
</tr>
</tbody>
</table>
SLE and Contraception

• Indications: active lupus, severe kidney disease, pulmonary hypertension, teratogenic medications

Types:
• Intrauterine device (IUD): ok for all lupus pts
• “The pill”:
  – Combined (estrogen+progestin)
    • Safe, if lupus stable/ inactive
    • Avoid in active lupus or in anti-phospholipid antibodies/syndrome (APS) (↑risk of blood clots)
  – Progestin-only pills or Depot shots are safe in SLE and APS
• Emergency contraception (“Morning-after pill”) is safe in SLE and APS
Monitoring of pregnant SLE patient

- Close follow-up with Obstetrician experienced with “high-risk pregnancies”
- Close follow-up with Rheumatologist
- Physical examination, blood pressure measurements
- **Urine tests**
  - Kidney inflammation
  - Protein in urine
- **Blood tests**
  - Blood counts
  - Liver function
  - Lupus antibodies in blood (Ro and La, dsDNA, antiphospholipid)
  - Complements (blood)
  - Uric acid (blood)
- Heart **ultrasound** of the baby (Fetal Echo)
  - if positive anti-Ro/SSA or anti-La/SSB antibodies in mother
  - Once a week, from weeks 16-26
What if my lupus flares up during pregnancy?

- Severity and organs involved

- Certain medications can cross placenta and affect baby

- Risk/benefit assessment
  - Uncontrolled lupus more threatening than medications

- Treatment of lupus should not be withheld because of pregnancy
  - Effort to minimize harm
### Differentiation of SLE flare from physiological pregnancy changes

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Pregnancy-related changes</th>
<th>SLE flare</th>
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<tr>
<td>Mucocutaneous</td>
<td>Facial flush</td>
<td>Photosensitive rash</td>
</tr>
<tr>
<td></td>
<td>Palmar erythema</td>
<td>Oral or nasal ulcers</td>
</tr>
<tr>
<td></td>
<td>Postpartum hair loss</td>
<td></td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td>Arthralgias</td>
<td>Inflammatory arthritis</td>
</tr>
<tr>
<td></td>
<td>Myalgias</td>
<td></td>
</tr>
<tr>
<td>Hematologic</td>
<td>Mild anemia, Mild thrombocytopenia</td>
<td>Leucopenia, lymphopenia</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Thrombocytopenia</td>
</tr>
<tr>
<td>Renal</td>
<td>Physiologic proteinuria $&lt;$300mg/day</td>
<td>Active urinary sediment</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Proteinuria $&gt;$300mg/day</td>
</tr>
<tr>
<td>Immunologic</td>
<td>Higher complement levels</td>
<td>Falling complement levels</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Rising anti DNA levels</td>
</tr>
<tr>
<td>Others</td>
<td>Fatigue</td>
<td>Fever</td>
</tr>
<tr>
<td></td>
<td>Mild edema</td>
<td>Lymphadenopathy</td>
</tr>
<tr>
<td></td>
<td>Mild resting dyspnea</td>
<td>Pleuritis</td>
</tr>
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</table>
Medications (I)

- **Plaquenil (Hydroxychloroquine):** take it throughout pregnancy (!!!)
  - Fewer lupus flares
  - Protects baby from mother’s antibodies (anti-SSA)

- **Steroids** (Prednisone, Medrol):
  - Ideally <10mg daily; ok at higher doses if needed for flares

- **NSAIDs** (e.g. Ibuprofen etc):
  - Avoid in 3rd trimester
Medications (II)

- **Azathioprine (Imuran):**
  - Relatively safe; dose <2mg/kg daily

- **Cyclosporine and Tacrolimus**
  - Relatively safe, benefit outweighs the risk

- **Biologics (Benlysta and Rituximab):**
  - Used with caution when necessary; not enough data

- **Blood pressure medications**
  - selected ones; check with your doctor
• Certain lupus medications can be **harmful to the baby**
  – Pregnancy should be avoided while taking them
  – Switch to safer meds before getting pregnant
Take-home messages (I)

• Lupus pregnancy is a high-risk one
  – Risks of medications for the baby
  – Risks of lupus complications for mother and baby (miscarriage, premature birth, preeclampsia, heart problems for baby)

• Pregnancy can have an impact on lupus
  – Flares may occur more during pregnancy (if uncontrolled lupus entering pregnancy)
  – Kidney function may worsen during pregnancy (if pre-existing lupus kidney disease with elevated Creatinine)
  – Risk is minimized with good planning ahead of pregnancy

• How to ensure a safe lupus pregnancy
  – Risk assessment by your Rheumatologist
  – Control of active lupus before pregnancy (>6 months)
  – Switch high-risk medications to safer ones
  – Close follow up with your Rheumatologist, OB/Gyn and Kidney specialist
Take-home messages (II)

• Medications
  – Work with your doctors to make necessary changes as appropriate
  – Plaquenil, prednisone, Azathioprine are relatively safe in pregnancy
  – Cellcept, Methotrexate, Leflunomide are NOT safe for baby

• Lupus patients with positive antibodies (Ro or La)
  – Special monitoring by Obstetrician with frequent ultrasounds

• Lupus patients with phospholipid antibodies (APS)
  – Aspirin and injectable blood thinner throughout pregnancy and after delivery

• Lupus and fertility
  – No evidence that lupus itself reduces fertility, if it is well-controlled
  – Some medications might (e.g. Cytoxan)

• Most women with controlled lupus can safely get pregnant and have healthy babies
  – planning ahead with your Rheumatologist is crucial
  – If active lupus, postpone pregnancy until controlled for >6 months
  – If active kidney lupus → treat it first
THANK YOU