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Lupus (Stephanie Keeling, Section Editor)

Contraception in Systemic Lupus Erythematosus (SLE)

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Abstract

Purpose of review To identify an approach for contraception use in systemic lupus erythematosus (SLE), we take an in-depth look at the available contraceptive methods for female patients, their safety profile and possible drug interactions.
Recent findings Among the possible options, long-acting reversible contraceptives (LARCs) are considered the most effective option and should be considered in most cases. Combined hormonal contraceptives (CHCs) can also be used safely, except in case of active SLE or those at increased risk of thrombosis. Progestin-only contraceptives (POCs), on the other hand, are considered good alternatives for patients who have contraindications to CHCs.
Summary Contraception is a crucial issue in SLE given the potential pregnancy risks associated with active disease and teratogenic medications. It is important for both physician and patient to consider when pregnancy is not ideal due to health reasons or not desired; hence, proper education and counseling should be provided regarding the effects of SLE on pregnancy, as well as contraception. Several contraceptive options are available, and it is essential to understand the benefits and potential risks of each method to ensure reliable use of the most effective contraception for SLE patients.

Introduction

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease with heterogenous clinical presentations and disease course. SLE has a well-established female preponderance, with a female-to-male ratio of 9:1 [1]. Some characteristic features point to the role of hormones, particularly estrogen, in the pathophysiology of SLE. For example, the incidence of the disease is highest in females between age 15 and 45 years (i.e. during the ovulatory period) and disease exacerbations are often seen in important times such as during puberty and pregnancy [2]. A two- to three-fold increase in

disease activity during pregnancy in some women with SLE has been well-documented in several publications [3–6], especially in women who conceived when they had active lupus [7, 8]. Furthermore, pregnant females with moderate to severe SLE have a higher incidence of disease flares and obstetrical and fetal complications [5]. These harmful effects can be attributed directly to SLE disease activity, along with the side effects of medications on fetal development [9].

Clearly, SLE is a condition whereby an unintended pregnancy can be detrimental to the health of mother and fetus. So, it is of the utmost importance that planned pregnancy in females with SLE should ideally occur during a period of disease quiescence [7, 8]. Because of the health concerns specific to pregnant SLE patients, the safe use of contraceptives has to be a subject of discussion during the disease course. Since many medications used to treat SLE have significant teratogenic potential, use of effective contraception is imperative if pregnancy is not desired.

Regardless, many patients with lupus have unprotected sex. Female patients often lean towards barrier-or-behaviour-based contraceptive methods to prevent unwanted pregnancy [10–12, 13••]. Previously, many women were counseled against using combined hormonal contraceptives (CHCs) based on two main concerns: (1) increased SLE flares and (2) cardiovascular and thrombosis risks [11]. In the last decade, many investigators have published reassuring data based on trials on the use of combined oral contraceptives (COCs) [14••, 15], progestin-only-pills (POPs) [14••, 16] and copper-releasing intrauterine device (IUD) [14••] on SLE disease activity during pregnancy.

This article discusses different aspects of SLE disease activity, contraception and pregnancy to present state of the art data on pregnancy planning and management in lupus patients. We present a brief overview of the types of contraceptives available, their safety profile concerning SLE disease activity in pregnancy, risk of thrombosis and interactions with concomitant drugs being taken for SLE itself.

Overview

Women with SLE seeking contraception should be counseled on the necessity of contraceptive use, as well as the full range of effective methods available. Contraceptive counseling should include a discussion of typical failure rates and the importance of using the contraceptive method consistently and correctly in order to avoid pregnancy [17•]. The choice of contraception must be individualized to each female patient with SLE and should be weighed against the potential benefits and risks taking into consideration the wishes of the patient.

Perfect versus typical use

When deciding a contraceptive method, it is vital to understand and focus on contraceptive effectiveness, which is related to "typical use" (i.e. reflecting real-world use). Contraceptive efficacy, on the other hand, demonstrates the "perfect use" of a method. The difference between failure rates of typical versus perfect use tends to decrease if a user-independent method is selected. Hence, the failure rates of typical and perfect use are nearly identical for long-acting reversible contraceptives

(LARCs), which are the most effective contraceptive option, as they require no effort on the part of the patient.

Contraceptive use prevalence and underutilization of effective methods/counseling

In general, women with SLE are at risk for unplanned pregnancy and do not consistently use contraception. Even when they do, they often do not use the most effective types or use CHCs despite a potential contraindication. A recently published large multi-national inception cohort in SLE ("SLICC cohort", n = 927) [18] reported that more than half of SLE patients using CHCs had one or more possible contraindication.

Another prospective observational study (n = 206) on use of contraceptive counseling in women with SLE [19] reported that barrier methods, which have a high failure rate with typical use (refer to Table 1), were the most common form of contraception used. This finding is consistent with a Finnish study that compared SLE patients with population controls and found that the use of effective contraception by women with SLE is relatively low [53, 54].

It is argued that the main approach to tackle these issues and to increase the use of effective methods is contraceptive counseling [54]. Moreover, interdisciplinary collaboration, by involving an obstetrician/gynecologist, is an important predictor of both contraceptive counseling and use [19].

Contraceptive methods

Many contraceptive options are available to physicians. Options discussed are based on the *Clinical Practice Guidelines: Canadian Contraception Consensus* [17•]. A detailed summary has been provided in Table 1. Each contraceptive option falls into different categories based on the three tiers of typical use effectiveness [55]. Specific names and choice of contraception options are also mentioned.

Impact on disease activity

The main precaution against using hormonal contraception in patients with SLE relates to SLE disease activity. The high female predominance in SLE during childbearing years has implicated estrogen in the development, and perhaps the worsening of the disease. In the past, many women were counseled against using CHC based on two primary outcomes of concern: a rise in SLE flares and risk of thrombosis [11]. These concerns were thoroughly studied in the last two decades, and of particular interest are two randomized controlled therapeutic trials published in 2005 [13••, 56••]. These trials evaluated whether the use of CHCs was associated with worsening SLE disease.

Table 1. Contraceptive options

Tier of effectiveness[a] (perfect use, typical use)	Methods	Characteristics	Side effects	Contraindications (CI)	Non-contraceptive benefits
IUC					
Tier I (99.9%, 99.9%)	Progesterone IUS	Contain Levonorgestrel LNG: Two choices available; Mirena 52 mg, Jaydess 13.5 mg. Very low failure rates that are comparable with permanent laparoscopic contraception. Considered the most effective methods of reversible contraception available in Canada [20–22, 23••].	Acne, breast tenderness, headaches, and altered mood. Risk of uterine perforation. Risk of PID in the first month of insertion. If pregnancy occurs with an IUD, increased risk of ectopic pregnancy	Absolute: Pregnancy, current PID, abnormal vaginal bleeding, malignant trophoblastic disease, current progestin receptor-positive breast cancer Relative: a history of progestin receptor-positive breast cancer, severely decompensated cirrhosis, hepatocellular adenoma, or malignant hepatoma, postpartum ≥ 48 h to < 4 weeks	The LNG-IUS 52 mg is also approved for the treatment of heavy menstrual bleeding (HMB) [24] associated with fibroids, endometriosis, adenomyosis [25, 26]. Associated with decreasing the risk of endometrial cancer [27].
Tier I (99.4%, 99.2%)	Copper IUD	Twelve different types of IUDs available in Canada (Mona Lisa, Liberte, Flexi-T, Nova-T). Considered the most effective methods of reversible contraception available in Canada [20–22, 23••].	Increase in menstrual blood loss. Risk of uterine perforation. Risk of PID in the first month of insertion. If pregnancy occurs with an IUD, increased risk of ectopic pregnancy.	Same as Progesterone IUS, except no risk of using in breast cancer or liver disease. Copper allergy	It is the most effective method of emergency contraception [28, 29]. Associated with decreasing the risk of endometrial cancer [27].
Hormonal					
Tier II (99.8%, 94%)	Depo-Provera (DMPA) Injection	150 mg/mL given as an intramuscular (IM) injection every 3 months.	Amenorrhea, disruption of menstrual patterns. Weight gain [30]. Delayed return of fertility [31]. A decrease in bone mineral density [32].	Absolute: Current diagnosis of breast cancer Relative: History of breast cancer, unexplained vaginal bleeding, severely decompensated cirrhosis, benign hepatocellular adenoma or malignant hepatoma	Approved for the treatment of endometriosis [33]. Reduction in dysmenorrhea and anemia. Reduced risk of endometrial hyperplasia and cancer [34]. Reduction of premenstrual syndrome and chronic pelvic pain [35].
Tier II (99.7%, 91%)	Combined oral contraceptive pills (COC)	Three types of estrogen are used in COCs in Canada: Ethinyl estradiol (EE), estradiol valerate(E2V), and 7 beta-estradiol (E2).	Abnormal uterine bleeding, nausea, weight gain, mood changes, breast tenderness, and headache.	Absolute: Known thrombophilia including antiphospholipid syndrome, SLE with positive (or unknown)	Combined oral contraceptive pills are associated with several of non-contraceptive benefits, including but not

Table 1. (Continued)

Tier of effectiveness[a] (perfect use, typical use)	Methods	Characteristics	Side effects	Contraindications (CI)	Non-contraceptive benefits
		Several different progestins are used in COCs, and most are 9-nortestosterone derivatives. Progestins may be classified according to their chemical structure as an estrane (norethindrone, norethindrone acetate, ethynodiol diacetate) or as a gonane (LNG, desogestrel, norgestimate). For an extensive list, refer to "Composition of Hormonal Contraceptives" [36•].		antiphospholipid antibodies, history of stroke, Severe decompensated cirrhosis [36•].	limited to decreased menstrual bleeding, decreased acne, fewer endometriosis-related symptoms, and a decreased risk of ovarian and endometrial cancers [36•]
Tier II (99.7%, 91%)	Transdermal patch	Delivers 200 µg of norelgestromin (the primary active metabolite of norgestimate) and 35 µg of EE daily to the systemic circulation. One patch is applied weekly for three consecutive weeks, followed by one patch-free week.	Same as COC, but comparatively it is associated with less breakthrough bleeding and spotting but more breast discomfort or pain, nausea and vomiting, and dysmenorrhea. Application site reactions also common.	Same as those for COC, exception is a history of malabsorptive bariatric procedures, which is not a contraindication to contraceptive patch use. Relative: Studies have suggested that the patch may be less effective in women with a bodyweight of ≥ 90 kg compared with women with lower body weights [37]	Similar to COC. Additionally, the patch has been shown to reduce pain symptoms in women with endometriosis [38]. It is also likely associated with improvements in hyperandrogenic symptoms such as acne and hirsutism [39, 40].
Tier II (99.7%, 91%)	Contraceptive ring	The contraceptive ring (NuvaRing available in Canada) releases 15 µg of EE and 120 µg of the progestin ENG (the active metabolite of desogestrel) per day, which is absorbed through the vaginal epithelium. After 3 weeks of continuous use, the woman removes the ring and has one ring-free week, during which time	The ring has similar side effects as the COC, except for more vaginal symptoms (vaginitis, leukorrhea, and ring-related problems).	Same as those for COC, exception is a history of malabsorptive bariatric procedures, which is not a contraindication to contraceptive ring.	Similar to COC. Additionally, it is associated with a decrease in menstrual blood loss, dysmenorrhea, migraines, and hirsutism.

Table 1. (Continued)

Tier of effectiveness[a] (perfect use, typical use)	Methods	Characteristics	Side effects	Contraindications (CI)	Non-contraceptive benefits
		withdrawal bleeding usually occurs			
Tier II (99.7%, 91%)	Progestin-only pill (POP)	POP is supplied in packages of 28 tablets, each containing 0.35 mg of norethindrone (Micronor or Movisse), with no hormone-free interval.	Menstrual cycle disturbances, worsening of pre-existing acne, headache, weight changes, and mood effects	Absolute: Current breast cancer Relative: History of breast cancer, severe (decompensated) cirrhosis, hepatocellular adenoma, malignant liver tumor	POPs containing dienogest (2 mg daily) is approved in Canada for the treatment of pelvic pain associated with endometriosis but not for contraception.
Barrier methods					
Tier III (94%, 88%)	Diaphragm	Currently three types available in Canada: Milex Wide-Seal Silicone Omniflex Diaphragm, Milex Arcing Diaphragm, (available by prescription in pharmacies and must be fitted by a health care provider. Yearly replacement recommended) and Caya SILCS Diaphragm (available at pharmacies or online without a prescription and can last up to 2 years). All three are to be used with acid buffering gel (Cayagel, Contragel).	Persistent or recurrent UTI [41], risk of TSS increases if in use for > 24 h [42].	Relative: Silicone/latex allergy and a history of TSS	None reported
Tier III (91%, 84%)	Cervical Cap	FemCap can be purchased online or with a prescription. Replacement is recommended every year. To be used with acid buffering gel (Cayagel, Contragel)	UTI (risk not as high as diaphragm) [43]	None reported	None reported
Tier III (98%, 82%)	Male condom	Latex, non-latex (polyurethane), natural lambskin. Ideally should be used in addition to another primary contraception method (dual contraception) [44•]. Most commonly used method of contraception by reproductive women in Canada.	Irritation, decreased sensation	Latex allergy	Decrease the risk of transmission of STIs associated with cervical/vaginal discharge (chlamydia, gonorrhea, trichomoniasis) [45–47]. Consistent condom use can decrease AIDS/HIV transmission by 80% [48].

Table 1. (Continued)

Tier of effectiveness[a] (perfect use, typical use)	Methods	Characteristics	Side effects	Contraindications (CI)	Non-contraceptive benefits
					May reduce premature ejaculation
Tier III (95%, 79%)	Female condom	Female condom FC2/FC1 can be purchased in pharmacies without a prescription. Should not be used at the same time as a male condom.	Invagination	Relative: Allergy to nitrile polymer, abnormal vaginal anatomy	None reported
Tier III (80%, 72%)	Spermicide	Nonoxynol-9 (N-9), a vaginal contraceptive film or as foam. Available without a prescription. Ideally should be used with another barrier method.	Vaginal and cervical irritation increase risk of HIV [49], UTI [50, 51]	Absolute: High risk of HIV. Relative: Allergy to N-9, HIV +ive/taking ART, history of TSS	None reported
Tier III (91%, 88%)	Sponges	Today sponge, a pillow-shaped sponge contains nonoxynol-9 spermicide, available in pharmacies without a prescription. Effectiveness can be increased by using the sponge in combination with a male condom	Risk of TSS [52]. Sensitivity to spermicide, and hence the risk of HIV, UTI.	Absolute: Same as spermicide Relative: Menstrual periods	None reported

Created by modifying "Contraception in Canada: A Review of Method Choices, Characteristics, Adherence, and Approaches to Counselling" Table 1 [58••]. The data has been gathered from the latest clinical practice guidelines of the Society of Obstetricians and Gynaecologists of Canada (SOGC) "Canadian Contraception Consensus" Table 2 [17•]

IUC intrauterine contraception, *LNG* levonorgestrel, *IUS* intrauterine system, *TSS* toxic shock syndrome, *CI* contraindications, *PID* pelvic inflammatory disease, *DMPA* depot medroxyprogesterone acetate, *IM* intra-muscular, *COC* combined oral contraceptives, *EE* ethinyl estradiol, *E2V* estradiol valerate, *E2* 7 beta-estradiol, *POP* progestin-only pill, *UTI* urinary tract infection, *STI* sexually transmitted illness, *AIDS* acquired immunodeficiency syndrome, *HIV* human immunodeficiency virus, *ART* antiretroviral therapy

[a]Effectiveness: % of women who do not experience a pregnancy within the first year of perfect/typical use

The first trial [13••] was a single-blind, randomized control trial (RCT) from Mexico which divided 162 patients equally in 3 groups (combined oral contraceptives (COCs), progestin-only-pills (POPs) and copper IUD) and found that overall, there was no difference in SLE global disease activity (measured by the Systemic Lupus Erythematosus Disease Activity Index [SLEDAI]), irrespective of the type of contraceptive they received. The second RCT [56••] was a double-blind, placebo-controlled trial in which 183 women with inactive (76%) or stable active (24%) lupus were randomly assigned to either COCs ($n = 91$) or placebo ($n = 92$). The authors of this study concluded that the occurrence of a severe flare was not different between the groups (7.7% in the COC group versus 7.6% placebo group). Furthermore, the 12-month severe flare rate was 0.084 for COCs and 0.087 for placebo, a difference of – 0.0028 ($p = 0.95$). Even though both clinical trials excluded women with severe disease and high risk of thrombosis, the results indicate that there is generally excellent tolerance of COCs concerning disease activity for women with inactive or stable active lupus.

These findings are further validated by two systematic reviews [14••, 57••]. The authors reported that based on available evidence, the use of COCs does not lead to increased flares of disease or worsening disease activity in women with inactive or stable active SLE. Hence, the benefits of use outweigh the potential risks.

Thromboembolism and contraceptives

Thrombosis and SLE

Venous thrombosis causes substantial morbidity and mortality in patients with SLE. In a review of studies relating to mortality in lupus, the three most common causes of death include infections, cardiovascular disease, and active SLE or associated organ failure [61]. According to a large cohort [62] based on multiethnic patients ($n = 1930$) from the Lupus Genetics Project [63], several risk factors significantly associated with venous thrombosis in SLE include positive antiphospholipid antibodies (aPL) (odds ratio [OR] 3.22, $p < 10^{-9}$), immunomodulatory medication use (OR 1.40, $p = 0.011$), nephritis (OR 1.35, $p = 0.036$), smoking (OR 1.26, $p = 0.011$), and longer disease duration (OR 1.26 per 5 years $p = 0.027 \times 10^{-7}$). Among these, aPL positivity is shown to be the most critical liability for venous thrombosis in SLE. Risk is highest among patients with lupus anticoagulant (LAC) and high titer immunoglobulin G anticardiolipin (aCL) [64]. Moreover, a large prospective study published in Canada [65] demonstrated that among patients with SLE who have LAC, as much as 42% will develop a venous thrombosis within 20 years of SLE diagnosis (95% confidence interval [CI] 21% to 63%, $p < 0.0001$). The authors of the study also concluded that LAC is a better predictor of risk for venous thrombosis than aCL.

Thrombosis and pregnancy

In women of reproductive age, over half of all venous thrombotic events are related to pregnancy [66]. Pregnancy is considered to be a hypercoagulable state since fibrin generation and levels of coagulation factors II, VII, VIII, and X are all increased, while fibrinolytic activity and free protein S levels are decreased [67]. The risk is considered to be highest during the 6-week post-partum period followed by the third trimester

[68]. This finding can be attributed to a reduction in venous flow velocity of approximately 50% occurring in the legs by 25 to 29 weeks of gestation and lasting until approximately 6 weeks after delivery, after which it returns to normal non-pregnancy flow velocity rate [69, 70]. Moreover, the increase thrombotic risk during pregnancy/postpartum period (73 in 10,000) is significantly higher than that associated with the use of CHCs (5 in 10,000) [71]. Therefore, it is essential to balance the risks associated with CHCs with the risks of unintended pregnancy.

Thrombosis and contraception

Combined hormonal contraception

Risk of venous thromboembolism (VTE)

Combined hormonal contraceptives (CHCs) have been shown to increase the risk of venous thromboembolism (VTE) [72]. This finding is well known in the general population; a meta-analysis in 2013 concluded that combined oral contraceptive (COC) use increased the risk of VTE fourfold [73]. The risk further increases in the presence of associated risk factors such as smoking, obesity, polycystic ovary syndrome, older age, immobilization [74], and thrombophilia [71]. Some women with SLE have hypercoagulability associated with antiphospholipid antibodies. Disease activity also increases the risk of VTE in SLE.

The progestin component of CHCs may affect thrombotic risk. Some studies [75, 76] have evaluated the differential thrombotic risk of third-generation (containing desogestrel, gestodene, or norgestimate) versus second-generation (containing norgestrel or levonorgestrel) oral contraceptives. The overall findings have substantiated that the thrombotic risk appears to be lower with second-generation progestins as compared to third-generation or unclassified COCs (drospirenone) [77, 78].

Myocardial infarction (MI) and stroke

A recently published meta-analysis reported a significantly higher risk of developing MI and stroke among COC users compared to nonusers [79]. Further evidence comes from a large multicenter population-based case-control study [80] (RATIO trial: Risk of Arterial Thrombosis in Relation to Oral Contraceptives), evaluating myocardial infarction (MI) and ischaemic stroke in women less than 50 years of age. For MI, the OR increased from 5.3 (95% CI 1.4–20.8) in the presence of lupus anticoagulant (LAC) to 21.6 (1.9–242.0) in the presence of LAC plus COCs. Similarly, the OR for ischaemic stroke was 43.1 (12.2–152.0) in the presence of LAC, which increased to 201.0 (22.1–1828.0) if there was a positive LAC plus COCs. Although prospective studies dedicated to the evaluation of the thrombotic risk of CHC use in patients with aPL are lacking, the results linking CHC

and venous thrombosis in the general population are in line with the safety data from the two RCTs in 2005 [13••, 56••].

Progestin-only contraceptives (POCs): progestin-only-pills (POPs), depot medroxyprogesterone acetate (DMPA) and levonorgestrel intrauterine system (LNG-IUS)

POCs are widely accepted as a lower-risk alternative to COCs for the general population. A meta-analysis [81] showed that collectively, they are not associated with increased risk of thrombosis compared with non-users (RR = 1.03, 95% CI 0.76 to 1.39). Moreover, in subgroup analysis, patients using POPs (RR 0.90, 95% CI 0.57 to 1.45) and LNG-IUS (RR 0.61, 95% CI 0.24 to 1.53) showed no significant increase in the risk of venous thromboembolism compared with non-users. On the other hand, DMPA was found to significantly increase the risk of developing thrombosis (RR = 2.67, 95% CI 1.29–5.53) when compared to non-users. However, due to the low number of DMPA users, the significance of this finding is uncertain.

Copper intrauterine device

The use of copper IUD in SLE has been evaluated in a RCT by Sanchez-Guerrero. Copper IUD (n = 54) was compared with COCs (n = 54) and POPs (n = 54) [13••], and although the risk of developing thrombosis was not studied as the primary outcome, it was reported as a secondary outcome. Patients in the copper IUD group did not develop any thrombotic event although the number of patients was small. However, a similar conclusion was reported in a follow-up review of this RCT [82].

Recommendations

Table 2 presents the recommendations for contraceptive use for women with SLE. These are based on the evidence-based medical eligibility criteria (MEC) put together by the World Health Organization (WHO) [59••] and United

Table 2. Summary of recommendations based on medical eligibility criteria (MEC) by the World Health Organization (WHO) [59••] and US Centres for Disease Control and Prevention (CDC) [60••]

Systemic lupus erythematosus	CHC	Copper IUD	POP	LNG IUS	DMPA	Implant
(a) aPL positive or unknown	4	1	3	3	3	3
(b) Severe thrombocytopenia	2	3	2	2	3	2
(c) Immunosuppressive therapy	2	2	2	2	2	2
(d) None	2	1	2	2	2	2

CHC combined hormonal contraception, *POP* progestin-only pills, *DMPA* depo-medroxyprogesterone acetate, *IUD* intrauterine device, *LNG-IUS* levonorgestrel releasing intrauterine system, *aPL* antiphospholipid antibodies

States Centres for Disease Control and Prevention (CDC) [60••]. They have assigned four categories to each medical condition: no restriction of use (level 1), expected benefit higher than risk (level 2), risks usually outweigh contraceptive benefits (level 3), unacceptable health risk if used (level 4).

Moreover, the United States Medical Eligibilty Criteria (US-MEC) [60••] has separated recommendation for depot medroxyprogesterone acetate (DMPA) and copper IUD into initiation (I) and continuation (C), signifying different risk and benefit in each scenario. Regarding initiation (I) of contraception, WHO [83••] and US-MEC [84••] recommend certain precautionary evaluations prior to beginning contraception (see Fig. 1).

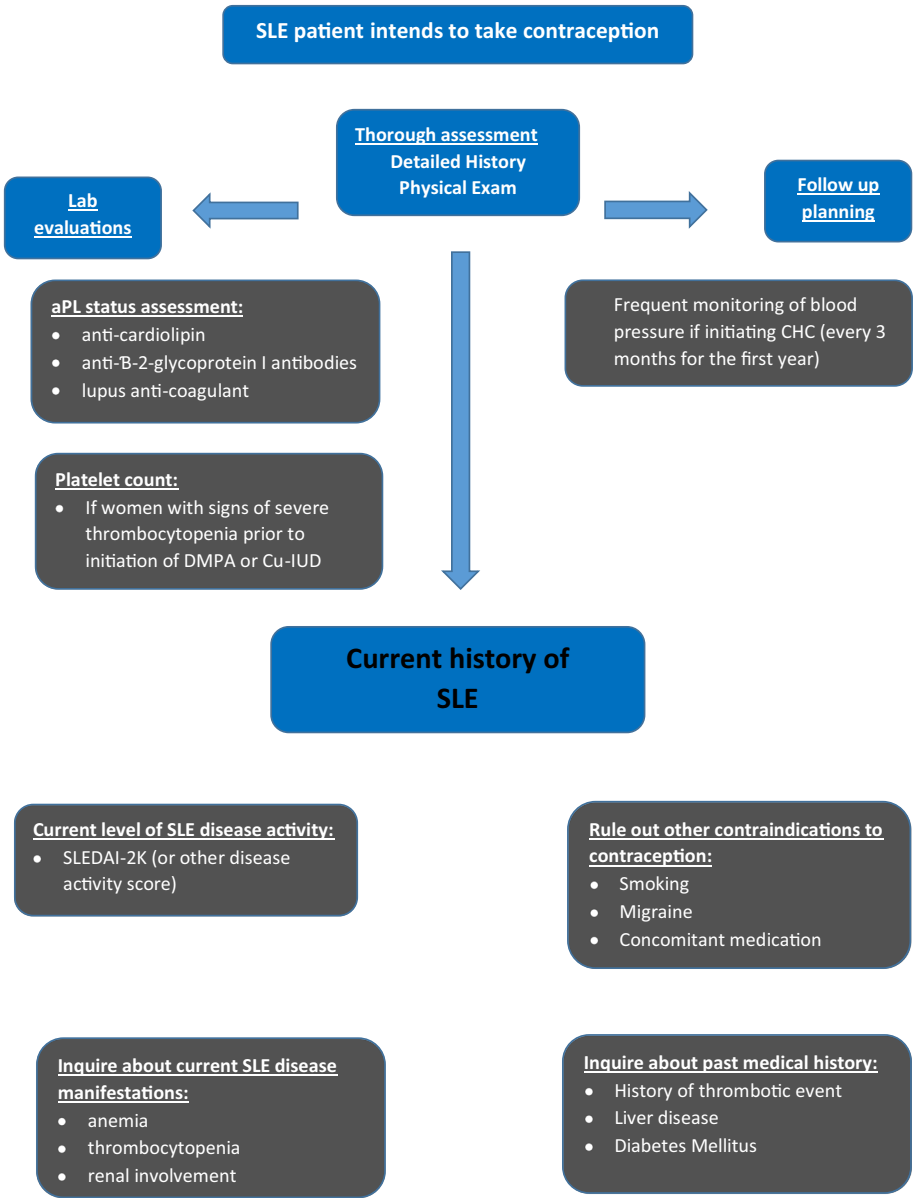

Fig. 1. Based on selected practice recommendation for contraceptive use (SPR)-US-MEC [84••].

Interactions with concomitant medication

Since a majority of patients with SLE are on multiple medications, it is important to identify and avoid any pharmacological interactions. These drug interactions are responsible for unplanned pregnancies as some result in decreased contraceptive efficacy.

Hormonal contraceptives are affected more by pharmacokinetic rather than pharmacodynamic interactions. The hepatic metabolism of ethinyl estradiol (EE) and progestins and their narrow therapeutic index makes them very sensitive to hepatic enzyme induction, the major risk being the decrease in contraceptive efficacy. Some medications may have potential interactions with CHC. For example, mycophenolate mofetil may reduce the efficacy of CHCs and preference should be given to progesterone eluting IUDs instead. CHCs may increase cyclosporine concentrations due to reduced metabolism requiring more careful side effect monitoring and possible dose reductions of cycloposporine. In the case of prednisone, CHCs may increase prednisone concentrations suggesting heightened awareness of possible steroid side effects and possible steroid dose reductions [85••, 86, 87].

Conclusion

Despite improvements in SLE including pre-conception and pregnancy and post-partum care, women with SLE are at most risk from harmful effects of pregnancy, especially if they conceive during active disease. Such pregnancies are associated with higher maternal morbidity and mortality, as well as poor fetal outcomes. Moreover, some medications used for the management of SLE are teratogenic or require careful use in the peripartum period. Considering these potential side effects, physicians should not be deterred from providing effective contraception in SLE.

When choosing between the various available contraceptive options, it is critical to recognize the contraindications, side effects, and potential for any drug interactions with concomitant SLE medications. Long-acting reversible contraceptives are considered to be the most effective and safest contraception available and should be encouraged even for patients with a history of thrombosis. Long-acting reversible contraceptives have the additional benefit of avoiding issues with compliance. Combined hormonal contraceptives are considered safe in stable-low disease activity and documented negative antiphospholipid antibodies, but are associated with a significant risk of venous thromboembolism and should be used after thorough assessment and evaluation for any contraindications. Progestin-only contraceptives provide a reliable alternative option for patients who cannot take combined hormonal contraceptives and who are not willing to use a long-acting reversible contraceptive. Despite a high rate of discontinuation due to irregular menstrual bleeding, progestin-only contraceptives are an effective option, and they are commonly used. Barrier methods are the least effective contraceptive method, and they should be reserved for situations when hormone-containing contraceptives or intrauterine devices must be avoided or are unacceptable to the patient.

Regardless, many women rely on contraceptive methods with relatively high failure rates. Therefore, it is recommended that patients with SLE are provided guidance regarding the effective and safe methods of contraception. Physicians should also facilitate access to interdisciplinary contraceptive counseling, which has been shown to increase compliance and use of effective methods.

Compliance with Ethics Guidelines

Conflict of Interest
Faizan Shaukat declares that he has no conflicts of interest. Stephanie Keeling declares that she has no conflicts of interest.

Human and Animal Rights and Informed Consent
This article does not contain any studies with human or animal subjects performed by any of the authors.

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- • Of importance
- •• Of major importance

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A single-blind randomized control trial (RCT) comparing the SLE global disease activity (SLEDAI) in 3 groups of patients, each group taking COCs, POPs, or copper IUD. This is an important RCT highlighting the similarity of SLE disease outcomes in each group regardless of contraceptive use.

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