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Autoimmune and connective tissue disorders

Anwar Nassar, Imad Uthman and Munther Khamashta

Pregnant women with autoimmune rheumatic diseases, especially systemic lupus erythematosus (SLE) and systemic sclerosis, are at high risk of maternal disease flares, adverse fetal outcomes and potential drug teratogenic effects, making the management of these women particularly challenging. With improvements in diagnosis and treatment, however, these risks can be minimized by appropriate timing of pregnancy and optimization of therapy before conception.

Preconception counseling represents a unique opportunity to optimize pregnancy outcome in women with chronic medical illnesses, those with autoimmune rheumatic diseases being no exception. This chapter reviews the impact of these diseases and their therapies on the mother and her fetus, the effect of pregnancy on these disorders with special emphasis on issues that should be discussed with women before they attempt to become pregnant, and measures that might be undertaken to optimize pregnancy outcome. The information provided can be used to counsel anxious mothers preconceptionally on what to expect during pregnancy and how to increase the likelihood of a successful pregnancy and the birth of a healthy infant.

SYSTEMIC LUPUS ERYTHEMATOSUS

SLE is the most common autoimmune disease affecting women during childbearing years, with a reported prevalence of 1 per 1000 women[1]. It is characterized by deposits of antigen–antibody complexes in capillaries and various visceral structures. Although once considered a contraindication to pregnancy, advances in disease management and perinatal monitoring now make pregnancy outcome in women with this multisystem, relapsing and remitting disease more favorable. Nonetheless, significant risk of morbidity to both the mother and fetus still may occur. No evidence suggests that SLE or any of the connective tissue disorders affect fertility, as ovarian failure is rare in these entities[2]. Prior treatment with alkylating agents such as cyclophosphamide is one of the risk factors for infertility; however, this risk is related to the total dose and the age of the patient at exposure[2–4]. Of interest, one population-based study has shown a smaller family size in women with SLE[5]. Ovulation induction appears to increase the risk of flare and thrombosis, especially in women with antiphospholipid (aPL) antibodies[6,7].

How does pregnancy affect SLE?

Pregnancy may exacerbate SLE activity[2,8] and increase the likelihood of maternal disease flares, which are reported to occur in 13.5–65% of pregnant women with SLE[8,9]. The most common SLE manifestations in pregnancy include constitutional symptoms and renal, skin and joint problems[8]. The risk of lupus flare during pregnancy is increased dramatically in women with active lupus in the

6 months prior to conception[2,10,11], whereas women in prolonged remission are less likely to experience an increase of lupus activity during pregnancy[12,13]. In a cohort of 267 pregnancies to women with SLE, the risk for significant SLE activity during pregnancy was significantly higher in women with disease activity shortly before conception (58% versus 8%; $p < 0.001$)[14]. Unfortunately, measuring lupus activity during pregnancy is not very straightforward, as some laboratory tests that are useful in non-pregnant women are less reliable during pregnancy[15]. Women with renal involvement are also at risk of deterioration in pregnancy, especially in the presence of hypertension, proteinuria (>1 g/24 h), glomerular filtration rate (GFR) <60 ml/min/1.73 m^2 and high baseline serum creatinine level at the time of conception[16,17]. Renal flares during or after pregnancy are observed in up to one-third of cases[16], and irreversible renal impairment is reported in 0–10% of these[18,19]. Some severe cases, albeit rarely, evolve to maternal death secondary to end-stage renal or multisystem failure[20,21]. Nonetheless, a recent multicenter study on 113 pregnancies occurring in 81 women with pre-existing biopsy-proven lupus nephritis suggested that pregnancy can be successful in most instances, even for those with severe renal involvement at onset of pregnancy[16]. Hypocomplementemia was the best predictor of adverse fetal outcome, and therapy with low-dose aspirin was significantly associated with better fetal and neonatal survival. Although pulmonary hypertension is uncommon in lupus, it confers a high risk of maternal death when it occurs in pregnancy[22,23]. Women on dialysis or with renal transplants can achieve successful pregnancy but have higher maternal and fetal complication rates[24].

How does SLE affect pregnancy?

Pregnancy outcomes have improved dramatically over the past 40 years, with the pregnancy loss rate falling from 43% in the 1960s to 17% by 2003, approximating the pregnancy loss rate in the general population in the United States[25]. In addition to spontaneous miscarriage, SLE is associated with increased risks of intrauterine fetal death (5–16%)[14], pre-eclampsia (13–35%)[19,26–28], intrauterine growth restriction (IUGR) (9–23%)[14,28] and preterm delivery (30%)[2,22,25,27,28]. These complications are more common in women with lupus nephritis, aPL antibodies, hypertension and in those with active disease at the onset of pregnancy[2,29]. Women with severe renal impairment (serum creatinine over 2.8 mg/dl) have less than a 30% chance of having a successful pregnancy[24]. Of the aPL antibodies, lupus anticoagulant is the most strongly associated with recurrent fetal loss[30]. Among women with SLE, the prevalence of aPL antibodies ranges from 15 to 30% for anticardiolipin antibodies and from 15 to 34% for lupus anticoagulant[31–34]. In addition, aPL antibodies in women with renal involvement represent a strong risk factor for thrombotic events, fetal loss and a worse renal outcome in long-term follow-up[34]. During pregnancy women with SLE are at particular risk of maternal venous and arterial thrombotic events, especially in the first 6 weeks' postpartum, with a reported incidence of up to 1.7%[35]. Evidence shows that aPL antibodies may further increase the risk for vascular thrombosis in women with lupus[36]. Other risk factors include hypertension, smoking and immobility. Clowse and colleagues recently reviewed the Nationwide Inpatient Sample, a large database with detailed information on 20% of all hospitalizations in the United States[35]. This is the largest study to date of SLE during pregnancy, reviewing more than 16.7 million admissions for childbirth over 4 years. Of these, 13,555 were to women with SLE. These investigators found an alarming 20-fold increased risk of maternal mortality in women with SLE (325 per 100,000 live births). In addition, the study confirmed previous reports of increased risks

of thrombosis, infection, thrombocytopenia, transfusion, preterm labor and pre-eclampsia. Morevoer, women with SLE also had a higher rate of cesarean delivery (36.6% versus 25.0%; OR 1.7, 95% CI 1.6–1.9), a finding in agreement with previous studies[26,37].

Neonates of mothers with the anti-Ro and anti-La antibodies may be affected by transplacental passage of these antibodies. This can range from cutaneous neonatal lupus – the most common manifestation of neonatal lupus observed in newborns of up to 4% of women with these antibodies[38] – to the most serious manifestation, i.e. congenital heart block. Although rare – affecting 2% of neonates of mothers with these antibodies[38,39] – this condition may be more common in women with hypothyroidism[40] and can result in intrauterine fetal death. It entails significant morbidity and even mortality, with almost all affected infants requiring pacemakers and a cumulative probability of survival at 3 years of age of 80%[41]. On the other hand, in the absence of active disease, hypertension, renal involvement, or aPL antibodies, women with SLE have a complication rate that approaches that of the general population[25,29].

Preconception counseling

Ideally, the management of pregnancy in SLE should be undertaken by a multidisciplinary team starting before conception and continuing throughout pregnancy in order to ensure the best obstetric outcome. The team should include but not be limited to a rheumatologist/internist, a maternal fetal medicine specialist with experience in management of women with SLE, and a nephrologist, depending on the woman's renal status. A preconceptional counseling visit is important to estimate the woman's risk profile, to discuss the potential complications and to establish an appropriate management plan.

SLE is not a contraindication to pregnancy with the exception of conditions that are associated with high maternal mortality rates, including pulmonary hypertension and renal failure[2,35,42]. For example, in women with symptomatic pulmonary hypertension, the risk of maternal mortality is estimated to be higher than 30%[43]. That having been said, the risk of complications during pregnancy is not uniform in all women with SLE. Women with active disease within the last 6 months prior to conception should be advised to avoid pregnancy[1,2,10,19,24] because this has been associated with an increased risk of lupus flare and poor pregnancy outcome.

Because women with SLE frequently require treatment throughout pregnancy, a thorough review of current medications is essential during the preconception visit[44]. Women should be instructed to avoid FDA pregnancy category X medications as well as most category D medications unless potential maternal benefits outweigh fetal risks.

Drugs that can be continued during pregnancy include prednisolone, azathioprine, cyclosporin A and hydroxychloroquine[2]. Corticosteroids have been used extensively and safely in patients with SLE during pregnancy. Azathioprine use in pregnancy is not associated with a significant increase in fetal abnormalities[45]. Most experts advise continuation of hydroxychloroquine in women contemplating pregnancy, as this medication decreases the risk of flares and improves the prognosis of SLE nephritis[2,45,46]. In fact, its withdrawal is frequently associated with subsequent flares in pregnancy[2,47,48] and the need for higher doses of corticosteroid therapy. In addition, hydroxychloroquine has a very favorable safety profile with no increased risk of fetal malformations identified in several hundred pregnancies exposed to it during the first trimester[45,47,49]. Methotrexate, mycophenolate mofetil (MMF) and cyclophosphamide are teratogenic and thus are contraindicated in pregnancy. MMF use during pregnancy is associated with an

increased risk of first trimester pregnancy loss and congenital malformations including those of the external ear and other facial malformations such as cleft palate and lip[50]. Cyclophosphamide is associated with a 16–22% risk of congenital malformations after first trimester exposure[45]. Women on any of these medications should be switched to safer alternatives such as azathioprine, as sudden withdrawal may precipitate a flare during pregnancy. Whereas some authorities recommend discontinuation of these medications at least 3 months prior to conception[2], others suggest a 6-month interval for stabilization of any preconception drug changes[51].

Traditional non-steroidal anti-inflammatory drugs (NSAIDs) are generally safe during pregnancy but should be avoided after 32 weeks of gestation because of their effect on the kidneys that may lead to oligohydramnios[52] and due to the risk of premature closure of the ductus arteriosus[53]. Antihypertensive medications are frequently prescribed in SLE. Women receiving angiotensin-converting enzyme (ACE) inhibitors and angiotensin-2-receptor antagonists should be switched to safer drugs like methyldopa and nifedipine before conception because of the associated fetal renal dysfunction, IUGR, anuria, renal failure and death with second and third trimester exposure[54]. Recently, fetal exposure to ACE inhibitors during the first trimester was also found to be associated with a risk of a major congenital malformation that was 2.7 times higher than that in fetuses exposed to other antihypertensive medications[55].

Women at increased risk for thromboembolic events should be identified, and those with positive aPL antibodies, particularly those with APS, should be started on thromboprophylaxis. However, exact dosages, time of initiation and durations of treatment that optimize fetal outcome have yet to be established[2]. Low-dose aspirin before conception if possible[56] seems to be a reasonable approach for prophylaxis against pre-eclampsia[57] and thrombosis, especially when combined with prophylactic dose low molecular weight heparin (LMWH) or unfractionated heparin at diagnosis of pregnancy[58]. Women with previous thrombosis might require full anticoagulation with LMWH or unfractionated heparin[59]. Women receiving long-term heparin should be supplemented with calcium and vitamin D to prevent osteoporosis[60].

Preconceptional medical evaluation should also include a precise review of the immunological status of the woman including lupus serology (dsDNA and nuclear antibodies), titers of anti-Ro/SSA and anti-La/SSB antibodies and aPL antibodies, serum complement levels (although these are less useful during pregnancy due to a natural increase of C3 and C4 levels[15]), renal function (creatinine, creatinine clearance and 24-h proteinuria) and evaluation of the blood pressure[58,61].

RHEUMATOID ARTHRITIS

Rheumatoid arthritis (RA), the second most common connective tissue disorder, affects women in their childbearing period with a prevalence of 1 per 2000[61]. RA does not appear to directly affect fecundity or fertility[62]; however, the lower pregnancy rates reported in these women can be explained by its psychosocial effects on childbearing choices[63,64].

How does pregnancy affect RA?

In contrast to SLE, disease activity in inflammatory arthritis such as RA usually improves during pregnancy[65,66]. Over 60% of women report improvement in pain and swelling, and some go into remission, as confirmed in the largest prospective trial on the impact of pregnancy and the postpartum period on RA[67]. The remainder show reduced disease activity in the second trimester, with fewer than 25% showing no improvement or deterioration during

pregnancy[1,67,68]. More recently, de Man and associates, using a validated scoring system, showed a 48% improvement in disease activity during pregnancy in women who had at least moderate disease activity in the first trimester, with a 27% remission rate in the third trimester[69]. Conversely, RA tends to relapse in the postpartum period in 39–70% of cases[64,67,69,70]. Aggravation of disease activity generally occurs within the first 6 months' postpartum[71] when almost all patients show signs of active disease[1].

How does RA affect pregnancy?

The impact of underlying RA on pregnancy outcomes is less well studied. Although some studies do not report any increased risk of adverse pregnancy outcomes in women suffering from RA in terms of rates of spontaneous abortion and risk of low birth weight[72,73], others report increased risk of hypertensive disorders of pregnancy[26,74,75], preterm delivery[72,75], cesarean delivery[26,72,75] and IUGR[26,75]. Reed and colleagues[72] reported on a cohort of 243 women with RA and found an increased risk for prematurity (adjusted relative risk (RR) 1.78, 95% CI 1.21–2.60), cesarean delivery (adjusted RR 1.66, 95% CI 1.22–2.26) but no increased risk for low birth weight after adjusting for gestational age[72]. Similarly, in a national survey of 1425 pregnancies in women with RA, significant increases in the rate of hypertensive disorders (11.1% versus 7.8%; $p < 0.01$), IUGR (3.4% versus 1.6%; $p < 0.01$) and cesarean delivery (37.2% versus 26.5%; $p < 0.001$) were reported. Severe hip arthritis may be an indication for cesarean delivery in some women with RA[76].

Preconception counseling

Women with RA should be evaluated prior to conception, when possible, in order to allow for conversion to safer pharmacologic regimens. Disease improvement during pregnancy often allows for safe discontinuation of potentially harmful agents. Medications that are safe in pregnancy include hydroxychloroquine, sulfasalazine, corticosteroids, NSAIDs prior to 32 weeks of gestation, and anti-tumor necrosis factor agents. Medications that are contraindicated include leflunomide and methotrexate. Since leflunomide may persist in the body for up to 2 years[77], the drug has to be discontinued and eliminated using cholestyramine at least 3 months before attempting pregnancy[64]. Similarly, most experts recommend discontinuing methotrexate 3–4 months before conception to prevent fetal exposure[64].

SYSTEMIC SCLEROSIS

Systemic sclerosis (scleroderma) is not commonly seen in pregnancy, as the mean age of onset is the mid-forties[78]. In these women, sexual functioning may be impaired secondary to Raynaud's phenomenon and dyspareunia[76]. To date, however, studies have not identified decreased overall fertility in these women, but little attempt has been made to relate the timing of pregnancy to the onset of the disease[79–81].

How does pregnancy affect systemic sclerosis?

In general, the disease does not deteriorate during pregnancy if the condition is stable at the time of conception[82]. In one prospective series, 61% of pregnancies had a stable course, 20% experienced some improvement, and 20% had some worsening of symptoms[81]. Symptoms related to systemic sclerosis, particularly Raynaud's phenomenon, improve during pregnancy, but esophageal reflux and shortness of breath on exertion may become worse, particularly during the third trimester[1,81,83]. The third trimester is probably the most critical

period for women with diffuse sclerosis secondary to the adverse effect produced by the enlarging uterus on pulmonary volume and renal function, both of which are already compromised by fibrosis[61]. Mallory–Weiss tears in women with esophageal involvement, who vomit during early or late pregnancy, have been described[1,84]. After pregnancy, some women with diffuse disease have increased skin thickening[81]. The worst complication of systemic sclerosis is renal crisis[85], which does not seem to be influenced by pregnancy[61]. This condition is more common in women with early diffuse systemic sclerosis and should be treated promptly and aggressively with ACE inhibitors despite their contraindication during pregnancy[1,85].

How does systemic sclerosis affect pregnancy?

Reports of pregnancy outcomes in women with systemic sclerosis are limited by the small sample sizes of the published data and conflicting results. Some studies report higher miscarriage rates[83,86] but this observation is inconsistent[79,81]. Case–control studies at single tertiary care centers have shown an increased frequency of preterm births and small for gestational age infants[83,86,87]. In the prospective scleroderma pregnancy study, 91 pregnancies in 59 women were studied[81]. No increased risk for small for gestational age infants was observed despite a significantly higher rate of preterm delivery (29% versus 5%). The overall live birth rate was 84% in women with limited systemic sclerosis, 77% in those with diffuse disease and 84% in historical controls. Earlier studies did not find higher rates of hypertensive disorders of pregnancy in women with systemic sclerosis[86,87]. Recently, however, Chakravarty and associates compared the pregnancy outcome of 504 women with systemic sclerosis to 11.2 million controls. Systemic sclerosis was independently associated with an increased risk of hypertensive disorders (OR 3.71, 95% CI 2.25–6.15) and IUGR (OR 3.74, 95% CI 1.51–9.28)[88].

Preconception counseling

A well-timed pregnancy with careful obstetric monitoring can maximize the likelihood of a successful outcome in women with systemic sclerosis. Because the incidence of a life-threatening renal crisis and other serious cardiopulmonary complications, such as severe cardiomyopathy (ejection fraction <30%), pulmonary hypertension, severe restrictive lung disease (forced vital capacity <50% of predicted), is higher in women who have diffuse sclerosis for less than 4 years, conception should be planned after this period[83,85]. History of renal crisis is not a contraindication to pregnancy provided that the disease has been stable for several years prior to pregnancy[1]. Medication adjustments are less problematic overall compared with other connective tissue disorders, because their use is not as common[76]. Histamine blockers and proton pump inhibitors may be used safely in pregnancy for the treatment of esophageal reflux, nausea and vomiting[89], and intravenous immunoglobulin therapy may be allowed, if needed[45]. Similar to other connective tissue disorders, hydroxychloroquine and corticosteroids can be used safely while cyclophosphamide is contraindicated.

ANTIPHOSPHOLIPID SYNDROME

Antiphospholipid syndrome (APS) is an acquired autoimmune thrombophilia diagnosed in the presence of characteristic clinical features including vascular thrombosis, obstetric complications and specified levels of circulating aPL antibodies, namely lupus anticoagulant and anticardiolipin antibodies. APS may be 'primary' or associated with other

autoimmune diseases, particularly SLE. A rare, life-threatening variant of the APS characterized predominantly by small vessel occlusive disease and multiple organ failure is referred to as 'catastrophic APS'. With advances in management, live birth rates of approximately 85–90% have been reported[90].

How does pregnancy affect APS?

Pregnancy is a prothrombotic state owing to increased hypercoagulability[91], hormonally induced decreased venous capacitance and decreased venous outflow[92]. The overall prevalence of thromboembolic events during pregnancy is approximately 2 per 1000 deliveries[93,94]. The risk of arterial thromboembolism, manifest as strokes and heart attacks, is increased three- to four-fold[93,94], while that of venous thromboembolism is increased four- to five-fold[95]. These risks are further aggravated in women with APS[96,97]. Another contributing factor to the increase in the incidence of thromboembolic phenomena in women with APS could be secondary to the discontinuation of warfarin derivatives upon diagnosis of pregnancy by some high-risk women on full anticoagulation due to the fear of fetal malformations. In addition to the increased risk of deep vein thrombosis, pulmonary emboli and stroke, and hepatic infarction have been reported in women with APS in pregnancy and the puerperium[1,98].

How does APS affect pregnancy?

APS is frequently associated with complications during pregnancy such as recurrent early pregnancy loss, as well as late second or third trimester fetal deaths[36,99–102]. Other adverse obstetric outcomes include pre-eclampsia, fetal death, IUGR and preterm delivery. Pre-eclampsia complicates 33–50% of pregnancies with APS[101,103,104]. It is not only more common in women with APS, but also tends to be more severe and to occur at earlier gestational ages compared with normal pregnancies[104,105]; some cases presenting prior to 20 weeks of gestation have been reported[98]. The HELLP syndrome, a specific complication of pregnancy characterized by hemolysis, elevated liver enzymes and low platelets, is more common and more likely to recur in subsequent pregnancies[106]. Although the incidence of HELLP syndrome in women with APS is unknown, Le Thi Thuong and associates[107] found that 53.3% of women diagnosed with HELLP syndrome had APS. IUGR complicates 15–30% of pregnancies in women with APS[103,108,109]. Preterm delivery prior to 34 weeks of gestation may be medically indicated in 37% of women with APS for maternal or fetal indications[103]. Other reported complications include systemic and pulmonary hypertension[42,60].

Preconception counseling

Treatment for APS usually consists of LMWH or unfractionated heparin in combination with low-dose aspirin throughout pregnancy and in the postpartum period, both agents being safe during pregnancy. Most experts advise starting low-dose aspirin (75–81 mg daily) preconceptionally and maintaining it throughout pregnancy. Aspirin has not been associated with an increased risk of congenital malformations[110,111], although some studies report a possible association with gastroschisis due to an increased risk of vascular disruptions[112–114]. Some women with APS and a history of thrombosis or cerebral events are maintained on long-term secondary prophylaxis with oral warfarin derivatives. Because of the known teratogenicity of these latter agents, it is advisable to switch from oral anticoagulants to adjusted dose heparin (either unfractionated or LMWH) before conception or with a positive early pregnancy test and to resume oral anticoagulation therapy postpartum[115,116]. The

preconceptional period is the ideal time to discuss these issues with women with APS.

CONCLUSIONS

Autoimmune and connective tissue diseases commonly affect women of childbearing age. Pregnancy in most of these women is at high risk for maternal and perinatal complications. An optimal obstetric outcome can be achieved only through coordination of care between the obstetrician, maternal fetal medicine specialist, rheumatologist/internist, and, in the case of renal involvement, a nephrologist (Table 1). The consultative process should ideally start prior to conception when women at high risk of pregnancy-related complications are identified and advised not to conceive or to delay conception until their medical condition permits. Medication lists may require some degree of modification in order to avoid the drugs of proven teratogenic effect. On the other hand, some drugs, such as low-dose aspirin, may be appropriate for a select group of women. Establishing a pre-pregnancy plan is

Table 1 The interplay between pregnancy and various connective tissue diseases (CTD)

	Pregnancy effect on CTD	*Effect of CTD on pregnancy*	*Preconception counseling*
Lupus	Exacerbation of disease in up to 65% of patients Risk factors: Renal involvement and active disease within 6 months of pregnancy Pulmonary hypertension: uncommon but increased mortality in pregnancy	**Fetal:** Fetal loss, IUFD, IUGR, preterm delivery, neonatal lupus **Maternal:** Pre-eclampsia, venous/arterial thrombosis, 20-fold increased maternal mortality, cesarean section **Risk factors:** Active disease, renal disease, hypertension, aPL	Pulmonary hypertension and renal failure: contraindication to pregnancy Avoid pregnancy if active disease within 6 months Check blood pressure, renal function, disease activity (complement levels) Assess thrombotic risk (aspirin/heparin accordingly) Check anti-Ro/La serology titers Safe drugs: steroids, azathioprine, cyclosporin A, hydroxychloroquine, NSAIDs*, methyldopa, nifedipine Drugs to avoid: methotrexate, mycophenolate mofetil, cyclophosphamide, ACE inhibitors, angiotensin receptor blocker

continued

Table 1 *continued*

	Pregnancy effect on CTD	*Effect of CTD on pregnancy*	*Preconception counseling*
Rheumatoid arthritis	60% Decreased disease activity/remission <25% No improvement 70% Relapse within 6 months postpartum	Inconsistent across studies Reported effects include: hypertensive disorders, preterm delivery, IUGR, cesarean section	Safe drugs: hydroxychloroquine, sulfasalazine, steroids, NSAIDs*, antitumor necrosis factor agents Drugs to avoid: methotrexate, leflunomide
Scleroderma	60% Stable disease 20% Improved symptoms 20% Worsening symptoms GERD+SOB: Worsen especially in third trimester Raynaud's symptoms: improve Renal crisis†: same as non-pregnant scleroderma population Increased skin thickness postpartum	Inconsistent across studies Reported effects include: miscarriages, preterm deliveries, IUGR, hypertensive disorders	History of renal crisis: not a contraindication for pregnancy Safe drugs: proton pump inhibitor, antihistamines, intravenous immunoglobulins, hydroxychloroquine, steroids Drugs to avoid: cyclophosphamide
Antiphospholipid syndrome	Increased venous/arterial thromboembolism	**Fetal:** Recurrent pregnancy loss (early-late), IUFD, IUGR, preterm delivery **Maternal:** Pre-eclampsia, venous/arterial thrombosis, HELLP syndrome, systemic and pulmonary hypertension	Treatment of antiphospholipid syndrome in pregnancy: aspirin and heparin Low dose aspirin started preconceptionally and maintained throughout pregnancy is advised Warfarin is teratogenic Patients maintained on warfarin therapy should be switched to heparin preferably preconceptionally

*NSAIDs are safe to use in pregnancy before 32 weeks' gestation

†Renal crisis in pregnancy as in non-pregnant patients is managed promptly and aggressively with ACE inhibitors

GERD, gastroesophageal reflux disease; SOB, shortness of breath; IUFD, intrauterine fetal demise; IUGR, intrauterine growth restriction; aPL, antiphospholipid antibodies; HELLP, hemolysis, elevated liver enzymes, low platelets; NSAID, non-steroidal anti-inflammatory drug; ACE, angiotensin converting enzyme

essential in order to anticipate possible complications, prevent them when possible or be ready to act on them as soon as they develop.

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