# Systemic Lupus Erythematosus

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Systemic lupus erythematosus (SLE) is an autoimmune disease of unresolved cause afflicting predominantly women in their childbearing years. Speculation exists as to the relative roles of viruses, histocompatibility loci such as HLA-DR3, and estrogen-mediated decreases in suppressor cell function.[1,2] Whatever the cause or familial tendency, the disease results in a pathologic hyperactivity of the B-lymphocyte population and a subsequent production of autoantibodies. This hyperactivity may reflect a primary B-cell defect or a deficiency of regulatory cells.[2,3] Although the pathogenesis of the disease has undoubtedly remained unchanged over the past 30 years, the diagnosis, maternal prognosis, and obstetric implications have changed. In 1955, Turner et al.[4] remarked that "Pregnancy is not a good omen for women with extensive lupus erythematosus." They expressed the hope that the introduction of adrenocorticotropic hormone (ACTH) and cortisone could prolong the lives of women affected by SLE. In 1974, Dubois et al.[5] demonstrated improved survival rates in association with high doses of corticosteroids. Although there has been a marked decrease in deaths from central nervous system (CNS) manifestations and uremia, fungal and opportunistic bacterial infections have become an important cause of death paralleling the increased utilization of steroids, dialyses, and transplantation therapies.

Because of increasing survivorship and the natural tendency for SLE to affect women of childbearing potential, an understanding of SLE in pregnancy is of growing importance to the obstetrician and the internist. To enhance such understanding, it is necessary for us to examine the interrelationships of the disease and pregnancy.

## Diagnosis and Manifestations

The diagnosis of SLE is often inhibited by its protean manifestations and its tendency to periods of exacerbation and remission. Specific preliminary criteria for standardizing the diagnosis of SLE were proposed by Chen et al.[6] in 1971. A proposed 1982 revision of criteria appeared in abstract form from Tan et al.[7] Both sets of criteria (Table 1) require the identification of four or more manifestations to establish the diagnosis of SLE with a high degree of sensitivity and specificity against rheumatoid arthritis, scleroderma, or nonrheumatic diseases.[6,7]

SLE manifestations vary, but arthralgias or arthritis present in roughly 90% of pa-

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TABLE 1. The Diagnosis of Systemic Lupus Erythematosus*

| 1971 Criteria[2] | Proposed 1982 Revision[3] |
|---|---|
| 1. Facial erythema, butterfly rash | 1. Malar rash |
| 2. Discoid lupus | 2. Discoid lupus |
| 3. Raynaud's phenomenon | 3. Photosensitivity |
| 4. Alopecia | 4. Oral ulcers |
| 5. Photosensitivity | 5. Arthritis |
| 6. Oral or nasopharyngeal ulceration | 6. Antibody to DNA or Sm or LE cells or false-positive STS |
| 7. Arthritis without deformity | 7. Proteinuria > 0.5 g/day or cellular casts |
| 8. LE cells | 8. Pleuritis and pericarditis |
| 9. Chronic false-positive STS | 9. Psychosis or seizures |
| 10. Profuse proteinuria > 3.5 g/24 hr | 10. Hemolytic anemia or leukopenia or thrombocytopenia |
| 11. Cellular casts | |
| 12. Pleuritis and/or pericarditis | |
| 13. Psychosis and/or convulsions | |
| 14. Hemolytic anemia or leukopenia or thrombocytopenia | |

*For each set of criteria, four or more are required for diagnosis of SLE.

tients. Dermatologic manifestations are seen in 70–80%, and renal disease is present in 46% of patients. Hematologic abnormalities are present in more than 50% of cases, but cardiovascular disease afflicts 30–50%.[8]

Of the hematologic aspects, anemia is the most common (57–78%) but is most often the anemia of chronic disease and not autoimmune in nature.[3] A positive direct Coombs test is relatively common, and leukopenia is seen in about 50% of patients. There is a greater absolute decrease in circulating granulocytes, in part secondary to marrow inhibition. A decrease in the absolute number and total proportion of T and B cells is seen, and the decrease in T cells reportedly parallels disease activity.[3] Lupus anticoagulant (IgG), sometimes associated with a chronic false-positive serologic test for syphilis (STS), interferes with activation of prothrombin by the prothrombin activator complex and inhibits clotting factor interaction on phospholipid surfaces.[9] The IgG fraction that contains lupus anticoagulant has been shown to reduce the release of prostacyclin and thereby plays a role in arterial thrombosis as well as the obstetric problem of reduced uterine blood flow and repeated intrauterine deaths.[9] Some manifestations of SLE may be altered by pregnancy. Tozman et al.[10] noted significantly less pleuritis and pericarditis and a suggestion of less CNS disease when comparing pregnant SLE patients with the total SLE population. In addition, Varner et al.[11] found the subset of patients in whom SLE developed in pregnancy had thrombocytopenia and heavy proteinuria more frequently. Indeed, can pregnancy cause an alteration in the onset or course, short-term or long-term, of SLE?

The first manifestations of SLE may occur during pregnancy or the puerperium. Both the initial diagnosis of SLE in pregnancy and the differentiation of preeclamptic toxemia (PET) from SLE nephritis can be extremely difficult.[11–16] PET is often associated with renal manifestations and may be present in 18–25% of all pregnant SLE patients.[12,14,16] Varner et al.[11] found that of the 18% of patients in whom symptoms of preeclampsia developed, 70% had their disease first diagnosed in pregnancy. Some feel that a renal biopsy in the third trimester is relatively contraindicated and the approach should be empiric.[14] Antinuclear antibody is not normally present in sera of normal or preeclamptic patients and may therefore aid in diagnosis.[15] Decreased gestational age (27–30 weeks), severity of hypertension, severity of renal involvement, anemia, thrombocytopenia, coagulation defects, and circulating antibodies may be atypical features suggesting a coexisting multisystem

disease.[11] Analysis of several studies[2,11,17,18] indicates that of all pregnancies complicated by SLE, 9-21% first had manifestations during pregnancy. Fine et al.[19] believe that this is not likely to represent an actual increase in the onset of SLE if compared with any 1-year period during the childbearing years.

## Effect of Pregnancy on SLE

There is no unanimous agreement as to the effect of pregnancy on the frequency of exacerbations or worsening of SLE nephritis. It is the current general feeling that a pregnancy conceived during a period of SLE remission is likely to remain quiescent. Conversely, it is less likely to undergo exacerbation.[18,20] If exacerbations do occur in such cases, they are usually mild.[18] Hayslett and Lynn[20] found of those in remission for 6 months before conception, the remission persisted in two-thirds; 32% had exacerbations, 10% severe but reversible in nature. If conception occurred during active SLE or lupus renal disease, the course was more severe. The manifestations worsened in roughly 50%.

The occurrence of exacerbations in different trimesters and the postpartum period varies widely in the literature.[8,10,11,13,14,17,28] Garsenstein et al.[25] formulated the relative risk of an exacerbation during either half of pregnancy or postpartum by comparing these periods to 32 weeks before conception and 9-40 weeks postpartum. The number of exacerbations or remissions per 100 weeks at risk was then calculated for each period. The relative risks were roughly 3.3 times those of the control period in the first half of pregnancy, 1.7 times those of the control period in the second half, and almost 7 times those of the control period in the postpartum period.[19]

Zulman[14] notes that SLE may have a profound short-term effect, noting in a literature review[12,14,17,25] that 19 of 20 maternal deaths occurred postpartum. The cause of such flares and remissions remains unknown, but they are probably dependent upon the degree of imbalance between trigger factors and regulatory factors. A postpartum drop in suppressive factors, a decrease in suppressor-cell activity or abnormal helper-cell function (or all three) could predispose a patient to altered disease activity.[2] In general, as opposed to pre-1970 reports, later studies show little or no increase in postpartum SLE activity. Zurier[29] comments that the characteristic increase in postpartum disease activity is apparently decreasing because more mild cases are being diagnosed. Additional factors include greater experience with steroid therapy and a greater general awareness of SLE.[29]

Bear[30] states that pregnancy may lead to serious and even lethal activation of SLE and/or lupus nephritis. However, most recent reviews indicate that pregnancy does not adversely affect the long-term course of SLE.[14,20,31,32] More specifically, evidence of disease activity in the 6 months preceding conception predisposed to permanent or transient renal function deterioration during or after pregnancy.[20] Yet in 61% of those same pregnancies antedated by the onset of SLE, the clinical course of the disease was not adversely influenced by pregnancy. This is in agreement with the findings of Zulman.[14] The long-term course of primary renal disease showed no evidence of pregnancy-related deterioration or lesion progression beyond that expected in the nonpregnant state.[32] In general, SLE patients who become pregnant have a more favorable prognosis than those who do not; however, this may well reflect disease severity as it relates to the capacity to become pregnant.[14,18]

## Effects of Pregnancy Termination on SLE

Having explored the effects of pregnancy on SLE, we shall consider the effects of pregnancy termination upon SLE. Donaldson et al.[12] noted that of 12 patients for whom therapeutic abortions were per-

formed for acute SLE, only 1 patient improved, 11 of 12 had no change or experienced disease reactivation, and subsequently 3 patients died. It is believed that for disease management, induced abortions exert little, if any, positive influence on subsequent clinical course,[21] and there is no evidence that therapeutic termination alone is "therapeutic" in a flare.[14] It will not prevent maternal morbidity.[19] By the same token, elective pregnancy termination should be an option for the patient. Zulman et al.[14] reported upon 10 patients who opted for elective abortions, including 1 with active disease, most of whom were given supplemental prednisone for 48 hours before returning to their regular dosage. In these cases, no detrimental short-term or long-term effects were noted.

## Maternal Effects of SLE

SLE exerts influences upon the mother. To the disappointment of physicians caring for patients 20 years ago when SLE was considered a "poor omen," it was noted that steroids did not prevent ovulation, although amenorrhea was sometimes seen.[18] Fertility was unimpaired when the disease was under control.[33] Several investigators[17,26,28] noted that sterility and fertility were virtually unchanged by maternal SLE. Fraga et al.[17] found that the overall fertility rate (pregnancies per fertile patient) prior to the clinical onset of disease was 3.4 and after diagnosis, 2.1. When compared with control subjects, however, the fertility of SLE patients was not seen to be significantly altered. Involuntary sterility was noted in 24.5% of patients after the diagnosis and in 25% of the control group. Although fetal effects of SLE are discussed later, it should be noted that SLE exerts an adverse effect on perinatal outcome *before* as well as *after* its diagnosis. In one study population, there were 23.1% spontaneous abortions prior to diagnosis and 40.5% following diagnosis. The control group rate was 12.5%. Maternal steroid therapy did not improve the abortion rate. It has been recommended that preclinical disease be suspected in mothers experiencing recurrent losses, particularly in black women.[31]

Patients with SLE have increased maternal morbidity and mortality. The risks of exacerbation as well as the increased risk of preeclampsia (18–25%)[12,14] were previously discussed. Houser et al.[23] found that only those patients in whom severe preeclampsia or nephritis developed exhibited changes in renal function status. Despite this finding, it was their conclusion that although the patient with lupus nephropathy has a high-risk pregnancy, the likelihood of an unfavorable outcome in patients without abnormal renal function or active SLE seems small. When under intensive medical and obstetric management, there was no long-term risk to maternal well-being.[23,26] Fine et al.[19] found that in 114 pregnancies, only 15 patients suffered permanent deterioration.[22] In patients in whom SLE developed in pregnancy, there was no evidence that the subsequent course would be different from that expected in the absence of pregnancy.

Earlier reports[4,28] stressed increased maternal mortality, particularly in the face of renal or cardiac disease. Subsequently, reports have shown that although pregnancy in SLE may exacerbate the disease, there is no proof that it leads to increased maternal mortality.[13,25] Furthermore, in patients with renal involvement, there was no significant difference in deaths due to lupus glomerulonephritis during pregnancy as compared with the nonpregnant state.[25] The subsequent maternal course is regrettably impossible to predict on the basis of the course of the disease during a prior pregnancy.[18]

## Fetoplacental Effects of SLE

SLE affects the fetoplacental unit before and after its clinical recognition. Fetal outcome is dependent upon disease activity.[20,21,23] Most authors would agree that pregnancy wastage is increased secondary to SLE.[11,15,17,19–21,23–25,27] Before diagnosis, spontaneous abortion estimates range up to 23–30%.[11,17] Following diagnosis, spontaneous

abortions occur in 5-40% of pregnancies.[11,17,19,27] The normal spontaneous abortion rate ranging from about 8% to 12.5%.[11,17] Fetal loss is further increased by sequelae of prematurity, which occurs in 16.6-37% of pregnancies following the diagnosis of SLE.[8,12,15,18,21,23,25] Estes and Larson[18] reported an increased risk of fetal death late in pregnancy, and estimates of stillbirths range from 12 to 30%,[12,22] with fetal wastage of 25-33.3%[12,21,22,24]

Loss is related to maternal disease activity.[11,19-21,23,25] With respect to lupus renal disease, a maternal serum creatinine of 1.5 mg/dl carried a 50% fetal loss rate,[20] and a maternal BUN greater than 50 mg/dl was associated with adverse outcome.[19] Houser et al.[23] found, in patients with previously documented lupus nephropathy, that all ten pregnancies without clinical renal disease or active SLE at conception delivered at term and experienced a benign neonatal course. In eight pregnancies with clinical renal disease or active SLE at conception, only one resulted in a term delivery, and three were premature. Fine et al.[19] found that although there was a minimal effect of pregnancy on renal involvement, fetal survival was greatly compromised. If proteinuria and decreased creatinine clearance were present, pregnancy wastage was increased to 80%. On the other hand, if patients with lupus renal disease were in remission for 6 months before conception, the rate of successful live births was 92% (comparable to normotensive gravidas with diverse types of renal disease).[20] The rate of prematurity did not exceed the expected rate.

Aside from pregnancy loss or prematurity, what other effects does SLE or its therapy exert upon the fetus? No study[11,13,19,20,23,25] found any increased incidence of congenital anomalies among viable pregnancies. Likewise, no increased anomaly rates have been related to steroid or immunosuppressive therapy. Concordant growth retardation has been reported in infants of mothers with SLE.[19] If one combines two recent series,[11,19] 13 of 62 (21%) infants were small for gestational age, 46 of 62 (74%) were appropriate for gestational age, and 3 of 62 (5%) were large for gestational age.

Even after going through the birth process, the infant may suffer sequelae related to maternal disease. Neonatal SLE is usually considered to be a distinct entity from "familial" lupus. The onset of familial lupus is usually later in life and, more variable in course, and related family members have hypergammaglobulinemia.[34] The two most common manifestations of neonatal SLE are dermatologic and cardiac in nature. Cutaneous lesions are erythematous, scaly, and atrophic, usually involving the face and upper thorax, with resolution by 12 months of age. Congenital cardiac involvement consists of atrioventricular block. It is unusual for an infant to have both manifestations.[35] Transplacental humoral factors (ANA) disappear within weeks.[15] Hematologic abnormalities such as anemia, leukopenia, and thrombocytopenia can exist concurrently or in the absence of the rash or congenital heart block (CHB).[35]

CHB has a poorer prognosis than the skin manifestations.[35] The underlying pathology is endocardial fibroelastosis, fibrosis of the conducting system, and secondary mitral insufficiency and/or small patent ductus arteriosus.[35,36] Fifteen to 20% of these infants have associated congenital heart defects.[37] The cause of this condition is speculative—perhaps it occurs because of transplacental passage of immune complexes or maternal antigens that stimulate the fetal immune system to form complexes. Injury may occur early in gestation (4-6 weeks) during a critical period of organogenesis, and the nodal anlage then fails to develop normally. Alternatively, the definitive atrioventricular node develops, is injured, and subsequently undergoes fibrosis.[38] These infants may require pacemakers,[36] but most who survive the neonatal period do relatively well.[39] CHB is a permanent but presumably nonprogressive insult.[25] In a review of 42 infants with neonatal SLE, only 2 of 23 with the cutaneous form were male, whereas 12 of 30 with the CHB form were male.[35] This study contrasts with the work of Oleinick,[40] who

found that proximal siblings of SLE patients had a decreased sex ratio (fewer males to females), but offspring of SLE patients do not have an altered sex ratio.[40,41] Just as immunologic factors may dictate the manifestations of maternal lupus upon the fetus, the placenta is subject to such influences and may also affect fetal survival.[42-45]

Bresnihan et al.[44] found that the incidence of lymphocytotoxic antibodies in sera of SLE patients was significantly lower during pregnancies ending in live births than those ending in spontaneous abortions. Furthermore, these lymphocytotoxic antibodies could be absorbed with trophoblastic antigens, perhaps explaining increased fetal loss. The data of Lom-Orta et al.[45] is in opposition to this, however. Placental histologic and immunofluorescent examinations have shown immune complex deposition along the trophoblast membrane and necrotizing decidual vasculopathy with fibrinoid necrosis.[42,43] This may represent one of many mechanisms resulting in placental ischemia, impaired placental development and function, and subsequent fetal growth retardation or death.[42]

## Management of Pregnancy and SLE

Avoidance of adverse fetal outcome and provision of safe maternal-fetal passage through pregnancy, labor, and delivery are the goals of every obstetrician and internist involved in caring for the pregnant SLE patient. Realizing these goals requires an understanding of the interactions of SLE and pregnancy, utilization of laboratory and clinical assessments, and a working knowledge of current drug therapy.

Routine obstetric laboratory work may aid in diagnosis or indicate disease activity. As discussed before, 50% of SLE patients have a hematologic abnormality,[8] usually anemia. Leukopenia, thrombocytopenia, and a positive Coombs are not uncommon.[3] A chronic false-positive STS serves as a major diagnostic criterion and is noted in some pregnant SLE patients.[6,7,11] A routine urinalysis and sediment examination are important tools, because renal disease is present in almost 46% of SLE patients.[8] Other generally available determinations such as serum creatinine, blood urea nitrogen (BUN), creatinine clearance, and urinary total protein have been related to fetal outcome.[19,20] Several,[10,14,21,24] but not all,[11,20,21] authors feel that serial complement levels are predictive of the course of the mother's disease.

Baines et al.[46] found that in normal pregnancies the third component of complement ($C_3$) and total hemolytic complement ($CH_{50}$) showed gradually increasing activity as pregnancy progressed following a significant depression in the first trimester. They questioned whether this initial decrease in complement resulted from increased antigen-antibody reactions associated with the allograft of pregnancy. In a study of complement levels in normal and preeclamptic pregnancies, it was found that complement levels in preeclamptics at delivery, 1 day postpartum, and at 6 weeks postpartum approximated the control levels.[47]

Zurier et al.[24] investigated serum complement levels in pregnancies complicated by SLE. Although they did not specifically correlate abnormal values with exacerbations, they noted that the mean complement values in all trimesters were slightly increased but within normal limits. Tozman et al.[10] reported that in inactive SLE, $C_3$ and $CH_{50}$ rose during pregnancy, but $C_3$ remained in the normal range. When SLE was active, the patients had significantly lower $CH_{50}$ levels at the onset and throughout pregnancy. Devoe et al.[21] examined the relationship of lupus activity and complement levels prospectively in 13 pregnancies and concluded that exacerbations were signaled by decreased or falling levels of complement. Remission states were reportedly associated with normal or near normal $C_3$ or $C_4$ levels. There was considerable variability in antinuclear immunofluorescent studies and anti-DNA (Farr) assays, leading to the conclusion that complement is more useful in assessment and prognosis than antinuclear

factors. It is interesting to note that a review of the data of Devoe et al.[21] shows that although exacerbations were associated with decreased complement levels in six of seven exacerbations, one patient had an exacerbation with normal $C_3$ and $C_4$. Furthermore, 6 of 26 times complement levels were obtained from patients in clinical remission, $C_3$ and/or $C_4$ were decreased. In total, 8 of 33 listed complement levels did not correlate with clinical disease activity. Varner et al.[11] looked at serial complement levels in 12 pregnancies and commented that $C_3$ did not correlate with the course of the disease in 5 of 7 pregnancies with SLE exacerbations. $C_4$ paralleled $C_3$ in 10 of 12 pregnancies. Hayslett et al.[20] believe there is a poor correlation between the results of serologic tests and disease activity. Serial anti-DNA titers are of limited usefulness in signaling exacerbations or predicting the course of the disease.[11] It would appear that clinical parameters and renal and hematologic studies are most useful in assessing the course of SLE in pregnancy as well as the need for medication alteration.[11,20]

Clinical obstetric precautions in pregnancies associated with SLE are similar to those required for competent care of other high-risk pregnancies. As in all pregnancies, early exhaustive efforts should be made to establish firm pregnancy dating. This is obviously important in view of increased prematurity[8,12,15,18,21,23,25] and its role in possible intervention decisions. Intrauterine growth retardation occurs in SLE,[11,19] and the early diagnosis and appropriate management of this hinges upon accurate obstetric dating. Serial ultrasonographic examinations may be indicated. In attempts to reduce the high rate of stillbirth,[12,18,22] fetal surveillance consisting of electronic fetal heart rate monitoring and estriol determinations should be instituted at a time when reliable interpretation and successful intervention, if indicated, is possible—usually at 30-32 weeks' gestation.[11] It is important to remember that steroids may affect fetal estriol production, but subnormal estrogen excretion in pregnant women receiving less than 75 mg of cortisol daily is indicative of fetal failure to thrive and subsequent growth retardation or stillbirth.[48] As in other high-risk pregnancies, careful fetal monitoring should be employed throughout labor. If a maternal antiplatelet antibody is present (as is also the case in ITP) a fetal scalp platelet count should be performed early in labor.[49]

Delivery for the patient with SLE should be individualized and in accordance with good obstetric practice. Although the cesarean section rate for SLE patients has been reported as high as 59%,[10] Varner et al.[11] noted a rate of 12.9% (the same as the overall institution rate). Delivery for the majority of pregnancies completing the second trimester was accomplished spontaneously or with elective low forceps.[11] SLE per se is not an indication for cesarean section. Furthermore, there is no evidence that cesarean section is of benefit in cases of CHB.[39]

Reduction of postpartum exacerbations with intrapartum and postpartum corticosteroid augmentation has been championed,[8] and its use has been frequently reported.[8,10,11,19,21,25] The usual dosage mentioned is 100-150 mg of intravenous hydrocortisone every 8 hours, in addition to the maintenance dosage until after the first postpartum day.[8,21] Although some[11] would question the effectiveness of augmentation in preventing a postpartum flare, most would favor its prophylactic use.[8,10,19,25] It is recommended that immunosuppression not be decreased in the postpartum period.[8,11]

Although dialysis[19] and plasmapheresis[50] may play a therapeutic role, immunosuppressive and anti-inflammatory agents form the mainstay of current SLE therapy. It is clear that since the introduction of corticosteroid therapy, 5-year survival has improved from 70% to 93%,[19] although corticosteroids have had no effect on pregnancy outcome.[18] Patients who conceive with active disease should receive steroid and, if necessary, immunosuppressive therapy as in the nonpregnant state.[14] It is agreed that there is no justification for alteration of needed therapy because of pregnancy.[11,19] Of

note, Varner et al.[11] found that of nine pregnancies in which disease worsened, four had been advised to decrease medication prior to the exacerbation.

Medical management of SLE can potentially produce undesired effects in pregnancy. Although the benefits outweigh the risks,[11,14] physician understanding and subsequent communication of the relative risks to patients is important. Aspirin is frequently used but may induce bleeding in patients with circulating anticoagulants. Furthermore, in a review, high-dose aspirin consumers had longer gestational length, longer labor, an increased incidence of postmaturity, and increased blood loss.[51] Cytotoxic drugs are sometimes used in pregnancy. Although the risk of a malformed viable infant following the first-trimester administration of a cytotoxic drug must be considered, no reproducible anomaly has been reported in humans. For drugs administered in the second and third trimester, the risk of a fetal malformation is no greater than normal. Importantly, 40% of babies born after cytotoxic drug administration are low in birth weight, and no follow-up studies of their fertility are available.[52]

Azathioprine is a purine analog, felt to be a "steroid-sparing" agent with less immunosuppressive and more antiinflammatory activity than cyclophosphamide.[51,53] Sudden withdrawal of azathioprine can cause a severe refractory exacerbation.[19,51] Follow-up karyotype examinations, intelligence testing, and neurologic examinations in infants of mothers receiving azathioprine have revealed no abnormalities.[53] The skeletal system of laboratory animals appears to be the primary target of azathioprine as a teratogen; yet only one case of pre-axial polydactyly has been reported in association with its use.[54] It appears that azathioprine use is relatively safe in pregnancy.[53,54]

Beneficial maternal effects of steroids were previously discussed, but with their use should come the realization that there is a relationship between corticosteroids and infection. Infection is now a leading cause of death among SLE patients.[5] Although glucocorticoids in combination with immunosuppressive drugs may cause decreased thymic size and a slight decrease in the neonatal lymphocyte count,[19] adverse fetal effects are rare. There have been a few reports of reduced fetal growth, but no report shows an increased human incidence of cleft lip or palate.[19] The human placenta converts a large fraction of prednisone and prednisolone to inactive 11-keto forms, but not dexamethasone or betamethasone.[55] The resultant concentrations of these steroids dictate that prednisone or prednisolone, not betamethasone or dexamethasone, be used to treat maternal diseases.[56] Prednisone and other steroids are secreted in breast milk. Although a maternal prednisone dosage of less than 30 mg/day is unlikely to create problems,[57] breast-feeding while on glucocorticoids or azathioprine is to be discouraged.[19,57]

## Family Planning

Traditionally, the postpartum period has been a time to discuss contraception and family planning. Warnings have been given that the increased exertion associated with child care may tax the mother and thereby increase her risk for increased disease activity.[58] To avoid undesired pregnancy, individualized careful consideration should be given to safe contraception. The fear has been expressed that the use of intrauterine devices, particularly in immunosuppressed patients, poses undue risk of infection.[11,58] Use may also result in increased tissue damage and elevated antibody formation.[58] Oral contraceptive pills have been associated with thrombosis, hypertension, and possible disease exacerbation. The use of the traditional condom plus a spermicide or diaphragm has seemed prudent. Recently, support for this view was produced.[58] In summary, the use of estrogen-containing compounds, even at low doses (30–50 μg), should be avoided in women with SLE. When reversible contraception is chosen because of the possible desire for future

pregnancy, mechanical methods should be tried initially. If this is not possible, pure progestogens may be valuable because of antigonadotrophic and antiestrogenic effects.[59]

Routine gynecologic care should include regular Papanicolaou (Pap) smears. In a recent series,[11] 3 of 38 pregnancies showed abnormal results in Pap smears, and all 3 women were using immunosuppressive agents. Immunosuppression is known to predispose the human cervical epithelium to dysplastic change.

## Conclusions

SLE in pregnancy is a high-risk condition for both the mother and the fetus, demanding intensive and aggressive obstetric and medical management. Through improvements in therapeutic regimens, more frequent diagnosis of milder cases, and diligent obstetric surveillance and management, the maternal and fetal prognoses appear to be improving. Ideally, patient education should occur at initial diagnosis; then pregnancies, if desired, should be planned during periods of remission. Educated about the maternal and fetal implications of the disease, the patient is better prepared both for the intensive observation needed and possible obstetric or neonatal complications that might occur.

Successful management of such pregnancies requires a team approach linking the obstetrician and the internist. It is recommended that patients with SLE in pregnancy undergo serial clinical evaluations using ARA criteria and careful scrutiny for development of PET. Maternal monitoring should include routine obstetric laboratory work as well as evaluation of hematologic and renal indices. Complement level determinations are favored by some, but the Farr assay appears to have little predictive ability. Careful pregnancy dating should be obtained, and fetal surveillance should be instituted as soon as the potential exists for fetal salvage. The route of delivery should be based upon appropriate obstetric indications. The postpartum period is a high-risk period for exacerbation of the condition, and prophylactic steroids may be beneficial in reducing this risk. Finally, it appears that barrier methods of contraception are the safest reversible forms of family planning for patients with SLE.

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