7-1980

The Effects of Pregnancy on Systemic Lupus Erythematosus

Julia Christensen

Abstract

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The safety of pregnancy for the woman with systemic lupus erythematosus (SLE) has long been studied. Controversy exists about the occurrence of exacerbations during pregnancy and the effect these exacerbations will have on the basic disease process. The purpose of this study was to investigate the effect pregnancy would have in precipitating exacerbation of disease activity. The investigation was carried out by comparing two matched groups of women with SLE, one group pregnant and the other group nonpregnant. The difference in occurrence of exacerbation among the three trimesters of pregnancy and the prepregnancy, pregnancy, and postpartum periods was also studied.

This nonexperimental descriptive case study used medical records of six pregnant (the study group) and six nonpregnant (the control group) women with SLE. The criteria for the sample selection was designed to eliminate as many extraneous variables as possible. All patients who met the sample criteria for the study group were included in the study. The records were then surveyed for all who met the criteria for the control group. The control group was then matched to the study group according to grade of disease activity; presence or absence of corticosteroid administration; age, plus or minus five years. Each medical record was reviewed for demographic data, past and present history of disease activity, and medications being taken.

When the six pregnant women with SLE were compared with the six nonpregnant SLE women, the occurrence of exacerbations was higher in the nonpregnant group. This may point to the fact that pregnancy does not always precipitate an exacerbation of disease activity. But because of the limitations of uncontrolled variables, sample size, difficulty in matching disease activity and length of time since original diagnosis, and imbalance in length of hospital records, generalization of this finding is impossible.

From the eight pregnancies reported, during pregnancy the only two exacerbations occurred during the third trimester, within six weeks of delivery. It was also found that of the prepregnancy, pregnancy, and postpartum periods, two exacerbations occurred during postpartum, two during pregnancy, and none during prepregnancy. These data suggest that if pregnancy were undertaken by the women with SLE the risk of exacerbation might be greatest during the third trimester and postpartum. The sample size of the present study, however, is too small to make such a generalization.

LOMA LINDA UNIVERSITY

Graduate School

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by

Julia Christensen

A Thesis in Partial Fulfillment

of the Requirements for the Degree

Master of Science in the Field of Nursing

July 1980

The persons whose signatures appear below certify that this thesis in their opinion is adequate, in scope and quality, as a thesis for the degree Master of Science.

Evelyn L. Elwell, Chairman
Evelyn L. Elwell, Associate Professor of Nursing

Annette M. Ross
Annette M. Ross, Associate Professor of Nursing

Grenith J. Zimmerman, Associate Professor of Biostatistics and Epidemiology

ACKNOWLEDGEMENTS

I would like to express my appreciation to the members of my thesis committee, Ann Ross and Dr. Grenith Zimmerman, for their support and assistance. I would also like to thank Dr. Linda Veneman and Ruth Brummer for their cooperation and assistance with the data collection process. Finally, I would like to thank Dr. Evelyn Elwell, my committee chairman, who gave liberally of her time, advice and encouragement.

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Chapter 1

THE PROBLEM

Introduction

A Caucasian female, age 21, became pregnant for the second time. The first child had been delivered without complication and the second pregnancy was uneventful until approximately 35 weeks gestation, when fever, proteinuria, and acute pulmonary edema developed. While in the coronary care unit on a ventilator, the mother delivered her second child. Five days postpartum a diagnosis of systemic lupus erythematosus (SLE) was made and steroid therapy was initiated. Her condition rapidly improved and she was discharged one week later on 60 mg of prednisone daily. A week later, at a clinic visit, her condition was so much improved that prednisone therapy was reduced to 15 mg daily. Two days later she was readmitted with pulmonary edema and gram-negative septicemia. She expired that day.

Delineation of the Problem

Systemic lupus erythematosus is a chronic inflammatory disease of unknown origin with deposition of immune complexes in several organs (Zurier, Argyros, Urman, Warren, and Rothfield, 1977, p. 178). The clinical manifestations vary widely as does the course of the disease. In most cases the disease pursues a chronic, irregular course marked by exacerbations and remissions. The relatively benign nature of the

disease is demonstrated by a 10-year survival rate exceeding 90 percent (Fessell, 1974, p. 1027).

It was not until 1971, when the American Rheumatic Association defined preliminary criteria for diagnosis of SLE, that there was any uniformity in diagnosis. With the discovery of the lupus erythematosus cell in 1948 and of other serological data, early recognition and treatment became possible. These recent discoveries coupled with a heightened awareness of diagnosis might partially explain the increased incidence of 1:700 in women 15 to 65 years old and 1:245 in black women 15 to 65 years old. Clearly SLE has replaced acute rheumatic fever as the gravest rheumatic disease (Fessell, 1974, p. 1030).

Systemic lupus erythematosus occurs four times more often in women than it does in men (Rodnan, 1973, p. 39). Onset most frequently occurs during the period of menarche to the menopause, with peak onset during the second decade (Estes and Larson, 1965, p. 308). Prevalence is therefore greatest for women during the reproductive years.

A review of the literature on the effects of pregnancy on SLE yields contradictory findings. Some investigators say exacerbations occur equally during both halves of pregnancy (McGee and Makowski, 1970, p. 1010), others that they occur in the second half (Zurier, and Others, 1978, p. 179), and still others that they occur during the first part of pregnancy (Friedman and Rutherford, 1956, p. 606). The majority of articles show exacerbation the rule during postpartum, although in two studies postpartum exacerbation was minimal or nonexistent (McGee and Makowski, 1978; Fraga, Mintz, Orozco, and Orozco, 1974). This reduction

in postpartum exacerbation has been attributed to the use of corticosteroids throughout pregnancy and/or high dose regimens prior to the onset of labor.

Since SLE occurs most frequently in women during the reproductive years, it would follow that questions concerning safety of pregnancy would frequently be asked of the nurse as the patient attempts to make decisions about her reproductive status. At present it is not clear what effect pregnancy has on SLE.

If a patient with SLE under good control and without evidence of renal disease should become pregnant could her disease become fatal? This question surfaces on examination of the literature, where two striking factors are reported: first, from the surveyed literature the reported maternal mortality rates ranging from 0-40 percent, and second, the number of women in which symptoms of the disease did not become apparent until they were pregnant or during the postpartum, 20.7 percent according to Fraga (1974) and 33 percent according to Garsenstein (1962). It appears that a seemingly quiescent disease process may be activated by pregnancy.

Research Questions

Because of the limitations of sample size and medical records this study was descriptive in nature and was concerned with research questions and their answers rather than with testing hypotheses. The three questions were as follows:

1. What effect will pregnancy have in precipitating exacerbation

of disease activity in women with SLE when they are compared with a similar group of nonpregnant women with the disease?

2. Is there a difference in the occurrence of exacerbations of SLE during the first, second, and third trimesters of pregnancy?

3. Is there a difference in the occurrence of exacerbations during prepregnancy, pregnancy, and the postpartum period of the SLE patient?

Conceptual Rationale

Systemic lupus erythematosus is considered an autoimmune disease characterized by an imbalance in the immune system. Bursa dependent (B) cell activity and antibody responses are excessive. Thymus dependent (T) cell activity or cell-mediated immunity is depressed. It appears that antibody production or suppression is controlled by helper T cells or suppressor T cells. Loss of suppressor T cell activity has been implicated as an underlying factor in pathogenesis of autoimmune disease (Krakauer, 1977, p. 56).

During pregnancy mixing of fetal and maternal blood may occur if placental blood vessels are torn during abortion or during late pregnancy. But the most frequent mixing occurs with disruption of fetal placental vessels during the third stage of labor (Willson, Beecham, and Carrington, 1975, p. 435).

It has been shown that pregnancy presents a new antigenic stimulus to the mother in the form of incompatible paternal HLA-antigens. Lymphocytotoxic antibodies have been detected in 20 to 50 percent of pregnancies,

depending on parity. It is suspected that their incidence increases not only with parity but with multiple paternity as compared to single paternity (Harris and Lordon, 1976, p. 302).

If these statements are true then an antigenic stimulus, such as incompatible fetal antigens released during late pregnancy or delivery to an already-abnormal immune system could precipitate an exacerbation of disease activity.

If pregnancy presents, as such, a serious threat to health stability, patients could be informed of such risks and be given alternative solutions to pregnancy. If pregnancy is desired, careful observation during pregnancy and postpartum could be planned with emphasis on compliance to a medical regimen.

Definition of Terms

The following terms are defined for the purposes of this study.

Systemic Lupus Erythematosus

A person presenting serially or simultaneously any four of the 14 preliminary criteria proposed by the American Rheumatism Association. See Appendix E for a listing of criteria.

Disease Activity

The level of disease activity classified by the following grades:

Grade 0. No systemic symptoms; no evidence of organ involvement.

Grade 1. One or two clinical manifestations which do not limit activities of daily living, including employment.

Grade 2. Two or more clinical manifestations which limit the patient in daily living, including employment.

Grade 3. Acute illness requiring hospitalization.

Exacerbation

An increase of disease activity by one or more grades.

Prepregnancy

The six-week period immediately preceding conception.

Postpartum

The six-week period after termination of pregnancy.

Abortion

Termination of pregnancy before the end of the twentieth week, either spontaneously or therapeutically.

Gravida

All pregnancies prior to the case being surveyed.

False-Positive Venereal Disease Research Laboratories (VDRL)

The presence of anticardiolipin antibodies in a patient with no clinical or historical evidence of syphilis, and whose serum fluorescent treponemal antibody absorption test is negative (Beeson, McDermott, and Wyngaarden, 1979, p. 514).

Anergy to Skin Tests

Reduced reactivity of the delayed-hypersensitivity skin testing

to common antigens such as tuberculin, mumps, streptokinase, and streptodornase (Beeson, and Others, 1979, p. 150).

Antinuclear Antibodies (ANA)

The presence of antibodies in nuclear material at any titer. A positive test supports the diagnosis of SLE, and a negative test is strong evidence against the diagnosis.

Lupus Erythematosus (LE) Cell

A traumatized leukocyte that releases nucleoprotein which reacts with an IgG antibody and is later phagocytized by the remaining viable leukocytes. LE cells are present in 75 to 90 percent of patients with SLE (Beeson, and Others, 1979, p. 178; Rodnan, 1973, p. 46).

Complement

Circulating inactive precursor proteins which, upon activation, mediate and amplify the inflammatory response (Beeson, and Others, 1979, p. 135). Complement levels are low when disease activity is present in SLE and reflect activation and fixation of complement components by circulating immune complexes. Levels of C_3 are often measured in hospital laboratories, although total complement and C_4 are preferred for following progression of disease activity (Bulmash, 1978, p. 172).

Apgar

Evaluation and scoring of the five objective signs (heart rate, respiratory effort, muscle tone, response to catheter in nostril, and color) at 60 seconds and again at five minutes after complete birth of

the infant. A total of 10 indicates an infant in the best possible condition (Vaughan, McKay, and Nelson, 1975, p. 334).

Limitations

Limitations of the study were as follows:

1. Rating errors by the data researcher with either overrating or underrating information.
2. Researcher bias.
3. Post-hoc error.
4. Nonrandom sampling.
5. Small sample size.
6. Unidentified extraneous variables.
7. Incomplete or inaccurate medical records.

Assumptions

The following assumptions were considered true for the purposes of this study. Some of these assumptions are currently controversial, and evidence may exist that they are or are not true.

1. The possibility exists that pregnancy can precipitate the onset of initial clinical manifestations of SLE (Fraga, Mintz, Orozco, and Orozco, 1974, p. 179).

2. Administration of corticosteroids decreases the percentage of exacerbations during pregnancy and the postpartum (Zurier, and Others, 1978, p. 179).

3. Incompatible fetal antigens released late in pregnancy or

delivery provide an antigenic stimulus for exacerbation of disease activity.

4. Surveyed medical records are well documented and reliable.

Organization of Remainder of the Study

Chapter 1 is a general introduction to the study. Chapter 2 reviews the literature and related studies. Chapter 3 presents the research method and the data collection procedures which were used. Chapter 4 presents and analyzes the data. Chapter 5 gives conclusions and recommendations.

Chapter 2

REVIEW OF LITERATURE

The reviewed literature has been classified under two general topics and will be presented in the following order: SLE and pregnancy, with emphasis on exacerbations; and precipitating factors of exacerbation.

Systemic Lupus Erythematosus and Pregnancy

The earliest references to lupus and pregnancy appeared in the literature in the 1950's. Donaldson first reported eight cases in 1952 and Friedman and Rutherford critically reviewed 29 cases in 1956. Between 1952 and 1971 a large number of studies were written before uniform criteria for diagnosis were proposed. Consequently, it is difficult to summarize and generalize findings because the studies have not separated systemic disease from discoid, and benign disease from either lupus nephritis or central nervous system manifestations. It is of interest to note that the majority of studies have been written by obstetricians, and criteria for differentiation of lupus are not mentioned. Currently, even with the establishment of uniform criteria, the complexity of the disease itself makes generalizations difficult.

Several studies are frequently cited because of their large sample sizes. Fraga reports 79 patients (Fraga, and Others, 1974, p. 294) and Friedman reports 80 patients (Friedman and Rutherford, 1956, p. 603).

The large sample size was used for the calculation of fertility potential, not for the course of SLE during pregnancy. In considering lupus and pregnancy, the researchers studied either a subgroup from the large sample or a small independent group. The sample sizes ranged from five to 36 patients except for 134 reported by Donaldson and deAlvarez (1962, p. 1464).

Another striking limitation of the eight studies reviewed is the absence of control groups in all but two studies. Fraga (1974, p. 294) utilized a control group, but it consisted of a comparable group of healthy females. This type of control may have been helpful in comparing fertility and fetal wastage rates, but for studying the course of lupus during pregnancy it lacked the type of relationship necessary for comparison. Garsenstein utilized a 32-week period before conception and nine to 40 weeks after delivery as control periods for each pregnancy (Garsenstein, Pollack, and Kark, 1962, p. 166).

In reference to the effects of pregnancy on SLE, the reviewed literature identified three important points. First, the high rate of initial onset of SLE occurred during pregnancy or postpartum periods. Estes and Larson (1965, p. 309) reported 17 percent with initial onset, Fraga (1974, p. 295) 20.7 percent, Garsenstein 33 percent (1962, p. 166). In Friedman's 29 patients with 24 pregnancies there were 13 cases of initial onset (Friedman and Rutherford, 1956, p. 606). If pregnancy precipitates onset of initial disease activity, the potential for exacerbation during pregnancy may be equally in force.

Second, the reported occurrence of exacerbation during pregnancy is contradictory, although recognition of postpartum exacerbation is

unanimously agreed upon. In Friedman's report of 29 patients, of which six had discoid lupus, there were 18 exacerbations during pregnancy, 10 during the first trimester, seven during the second, and one during the third trimester. There were 18 exacerbations postpartum plus eight cases of initial onset of disease activity. The number of remissions nearly equaled the number of exacerbations during pregnancy. From these findings he concluded that pregnancy did not alter the basic course of lupus and that those patients whose disease progressed during pregnancy would have experienced a progression despite the pregnancy. This may seem a logical conclusion, but the absence of a control group makes such statements inconclusive (Friedman and Rutherford, 1956).

Donaldson and deAlvarez's study concluded with results similar to Friedman's. In this sample of 105 patients (excluding those with discoid lupus) with 153 pregnancies, the majority had no change in their disease status nor an improvement. Exacerbation occurred in 24 cases during pregnancy. During the postpartum period 59 cases showed no change in disease activity, 21 cases improved, and 48 has exacerbations. The researchers felt that pregnancy does not aggravate the basic disease process and that the high rate of postpartum exacerbation is related to withdrawal of 17-hydroxycorticosteroids elaborated as pregnancy advances (Donaldson and deAlvarez, 1962). When one examines the study design a question arises about generalizing these findings. Of the 134 patients, including those with discoid lupus, it is noted that for 112 the data were obtained from a questionnaire sent to obstetricians and gynecologists. The seven-question questionnaire asked general questions relating to pregnancy and disease

activity without offering specific objective criteria. Data from medical records were obtained from only 22 patients.

Estes and Larson found results similar to those of the above studies. A retrospective study of 79 pregnancies in 36 patients concluded that pregnancy does not alter the course of SLE in the majority of cases. Exacerbations were associated with 18 pregnancies, none in the first trimester, four in the second, three in the third, and 11 in the postpartum period. They concluded that pregnancy may be undertaken in the absence of renal disease or hypertension without undue risk to the patient. They recommend close observation into the third month postpartum in view of the tendency for postpartum exacerbation (Estes and Larson, 1965).

Garsenstein and others studied 33 pregnancies in 21 patients. For analysis pregnancy was divided into two 20-week periods and a third period consisting of the first eight weeks postpartum. Two control periods consisted of 32 weeks prior to conception and from nine to 40 weeks after delivery. From these data, the number of exacerbations and remissions per 100 weeks of risk was calculated. During the first 20 weeks the risk of exacerbation was three times as great as in the control periods. In the second 20 weeks the risk decreased to 1.7 times the control, but most strikingly it increased to seven during the postpartum period. Sixteen patients were treated with prednisone throughout or for part of the pregnancy, while in 17 cases no prednisone was given. Of the group that received no prednisone 16 exacerbations occurred during pregnancy and 11 in the first eight weeks postpartum. In the 16 treated cases only eight exacerbations occurred during pregnancy and five postpartum. From these

data the authors concluded that pregnancy increases the chances of exacerbation of SLE, particularly during the first half of pregnancy and first eight weeks postpartum. These results are similar to those of Friedman and Rutherford. The latter concluded that the postpartum decrease in the serum level of 17-hydroxycorticosteroids occurs too early after pregnancy to be the sole explanation for the increased number of exacerbations four to eight weeks after delivery. It was also concluded that prednisone does decrease the rate of exacerbation (Garsenstein, and Others, 1962).

McGee and Makowski studied 11 pregnancies in seven patients to evaluate the effectiveness of therapeutic programs in the management of SLE during pregnancy. Corticosteroids were used to control symptoms during pregnancy. In addition, all patients treated with corticosteroids during pregnancy received a high dose of oral and intravenous steroids at the onset of labor. Intravenous therapy was discontinued the first postpartum day, but the oral corticosteroid was continued until three weeks postpartum and then gradually tapered in accord with clinical and laboratory data. Five of the 11 pregnancies had no change in symptoms. Exacerbations occurred in equal numbers during the first and second halves of pregnancy. No maternal deaths and no postpartum exacerbations were encountered. The authors felt that these data suggest that high-dose corticosteroid therapy during the intrapartum period is effective in preventing postpartum exacerbation (McGee and Makowski, 1970).

Similar reductions in postpartum exacerbations were reported by Fraga and others (1974) and Zurier and others (1977). A retrospective

study of 42 pregnancies in 20 patients by Fraga showed no exacerbations during the first trimester, three during the second, two during the third, and two postpartum, for a 13.2 percent exacerbation rate. Thirty-three of the pregnancies were treated with corticosteroids and nine were not. In the nine who were not treated, two maternal deaths occurred. None of the patients improved or had a remission. The authors' recommendation is that pregnancy be permitted during a clinical remission or well-controlled disease and that steroid therapy be utilized to reduce exacerbations (Fraga, and Others, 1974).

Zurier and others retrospectively surveyed 27 pregnancies in 13 patients and reported six exacerbations during the second half of pregnancy and three during the postpartum period, for an 11.1 percent exacerbation rate. Nineteen of the 27 pregnancies were treated with various doses of prednisone (5-60 mg/day) during pregnancy and 16 were treated throughout the entire course of pregnancy (Zurier, and Others, 1978). From these studies come contradictory conclusions about the occurrence of exacerbations of SLE during pregnancy, although there appears to be a definite increase in postpartum exacerbation.

The third point illuminated in a review of the literature is the fact that despite the number of exacerbations, maternal mortality rates are not increased except for patients with lupus nephritis. In an attempt to further differentiate the effects of pregnancy and lupus nephritis, Bear studied six pregnancies in five patients with quiescent lupus nephritis. Proteinuria increased during five of the six cases, with three progressing to heavy proteinuria without response to prednisone.

Two patients with heavy proteinuria died within two years of delivery despite prednisone and azathioprine therapy. The one patient with no change in proteinuria received prednisone throughout pregnancy, 15 mg/day. The author concluded that pregnancy deals a further insult to renal integrity with heavy and persistent proteinuria (Bear, 1976). Similarly, Estes found a progression of renal disease during pregnancy in all patients with lupus nephritis. Of 10 pregnancies associated with renal disease, five patients reverted to a prepregnancy state of renal disease, three had a stabilization in renal disease, and two progressed to death within one year of delivery (Estes and Larson, 1965, p. 316). McGee and Makowski also noted a decrease in renal function despite corticosteroids during pregnancy, but all cases improved after eight weeks postpartum (1970, p. 1012). In Garsenstein's study there were four maternal deaths, 19 percent. All four patients had lupus glomerulonephritis. None were treated with corticosteroids. The authors compared the number of deaths in both the pregnant and the nonpregnant patients with lupus nephritis and found no difference (Garsenstein, and Others, 1962, p. 168). In the studies reviewed, the maternal mortality rate ranged from 0-40 percent with the majority of deaths from progression of lupus nephritis.

Precipitating Factors of Exacerbation

The factors precipitating exacerbation of SLE during pregnancy are unknown. Possible explanations could include the rapid decline in cortisol levels following delivery and/or a hypersensitivity immune response stimulated by paternal fetal antigens.

In the literature reviewed in the previous section two references discussed the relationship of exacerbation to 17-hydroxycorticosteroids secreted during pregnancy. Donaldson and deAlvarez felt that the loss of the suppressive effects of the corticoids postpartum could precipitate the high incidence of postpartum and postabortal exacerbation (1962, p. 1468). Garsenstein and others felt that the lack of 17-hydroxycorticosteroids occurred too soon after delivery to account for the incidence of exacerbation seen four to eight weeks after delivery (1962, p. 169).

Total plasma cortisol and cortisol-binding globulin levels increase during pregnancy. Under normal conditions 90 percent of serum cortisol is bound to a specific binding globulin, namely, the corticosteroid binding globulin (Brien and Dalrymple, 1976, p. 361). It is the nonprotein bound or free cortisol that is the metabolically-active form of cortisol. Historically controversy has existed about the levels of plasma bound and free cortisol during pregnancy. The recent literature reviewed all supported the fact that nonprotein-bound cortisol increases during pregnancy (Doe, Dickinson, Zinneman, and Seal, 1969, p. 760; Galvao-Teles and Burke, 1973, p. 738; Brien and Dalrymple, 1976, p. 362). Doe and others noted that a cortisol-like aminoaciduria was present in pregnancy and felt that clinical symptoms such as purplish striae, easy bruising, hypertension and fluid retention were consistent with a mild cushingoid state (1969, p. 764). Brien and Dalrymple, measuring cortisol levels in 23 pregnant women at four-week intervals during pregnancy and six weeks postpartum, found that total plasma cortisol and free cortisol were significantly elevated by 12 to 15 weeks

of gestation and continued to rise throughout pregnancy. Bound cortisol was significantly elevated by 12 to 15 weeks, peaked at 20 to 23 weeks, and fell slowly thereafter until term (1976, pp. 362-363). None of the studies measured cortisol levels on a daily basis postpartum to determine the fall of plasma cortisol. Gemzell measured the level of 17-hydroxycorticosteroids six days after delivery and found them within normal range (1953, p. 901). Brien and Dalrymple measured cortisol levels at six weeks postpartum and found all parameters at nonpregnant levels (1976, p. 363). The fall of plasma cortisol postpartum with a resultant loss of anti-inflammatory and immunosuppressive effects may contribute to exacerbation.

Lack of rejection of a fetus which possesses both maternal and paternal genes is an enigma to those studying the immunology of pregnancy. The fact that maternal sensitization does occur in response to fetal antigens can be demonstrated by various laboratory methods. Terasaki, Mickey, Yamazaki, and Vredevoe demonstrated maternal sensitization by measuring lymphocytotoxic antibodies. They found 16.7 percent of women after one pregnancy developed cytotoxic antibodies, 23.6 percent after two, 36 percent after three, and 44.5 percent after four. Around the fourth pregnant a plateau was reached (1970, pp. 539-440). In studying 85 primiparous mothers Thilikainen, Schroder, and de le Chapelle found 22 percent developed cytotoxic antibodies to paternally derived antigens (1974, p. 356).

Another laboratory method utilized to evaluate the cell-mediated immunological response to fetal antigens was the assay of the macrophage

migration inhibitory factor, which is elaborated from sensitized lymphocytes. The serum of five of 10 pregnant patients with differing parity produced a migration inhibition factor when it was incubated in the presence of their infants' lymphocytes. All five of the mothers whose lymphocytes were sensitized to those of their infants had been pregnant three or more times (Rocklin, Zuckerman, Alpert, and David, 1973, pp. 130-131). In a similar study of five mothers with three or more pregnancies, lymphocytes produced migration inhibition factor in three of five mothers in the third trimester and five of five mothers in the postpartum. The migration inhibition factor was produced only in the presence of homologous pregnant plasma; when autologous plasma was utilized no migration inhibition factor was produced. This suggests that maternal sensitivity to paternal antigens is blocked by some factor in autologous maternal plasma (Pence, Petty, and Rocklin, 1975, p. 526).

These studies support the fact that maternal sensitization to paternal fetal antigens does occur. Since the presence of antibodies increases with parity one wonders if maximum antigenic stimulus occurs immediately prior to or during labor when fetal and maternal blood mix as separation of placenta from uterus occurs (Willson, and Others, 1975, p. 435).

Systemic lupus erythematosus is a disease in which the regulation of immune response is abnormal. An antigenic stimulus in the form of paternal fetal antigens delivered to the maternal circulation during labor could precipitate exacerbation of disease activity.

Chapter 3

METHODOLOGY

The nonexperimental case study method was used in this study. Data were obtained from the medical records of 12 patients from two hospitals. The records were surveyed between May, 1979, and June, 1979.

Selection of Sample

The target population for the study included SLE women hospitalized for pregnancy, where pregnancy occurred after the initial diagnosis of SLE, and/or evaluation of disease activity. Medical records from one 500-bed university medical center and one 250-bed county hospital were reviewed from the years 1968 to 1978.

Criteria for Selection of Sample

Patients were included in the study if they met the following general criteria:

1. Female.
2. Age 16 through 45.
3. SLE diagnosed according to American Rheumatism Association criteria (see Appendix E).

Patients in Group A, the study group, met the following additional criteria (at least four patients required):

1. Documented history of pregnancy past 16 weeks gestation.
2. Diagnosis of SLE prior to pregnancy.

Patients in Group B, the control group, met the additional criteria of no history of pregnancy (at least four patients required).

All patients who met the sample criteria for Group A were included in the study sample. The records were then surveyed for all who met the criteria for Group B. Group B was then matched to Group A according to grade of disease activity, presence or absence of corticosteroid administration, age plus or minus five years. The time period used for comparison was a period of relative disease stability prior to the surveyed pregnancy for Group A and prior to exacerbation in Group B.

Uncontrolled Variables

Variables that may have existed and affected the study include the following:

1. Incorrect diagnosis of SLE, despite utilization of diagnostic criteria.
2. Incorrect or incomplete medical records.
3. Patient noncompliance to medical regime.
4. Illnesses other than those associated with SLE.
5. Additional medical/social history pertinent to the case.
6. Length of medical record available.

Collection of Data

After sample selection each medical record was reviewed by means of a data extraction checklist (see Appendix F). In each case the entire medical record was reviewed for pertinent data, often far in excess of that required from the checklist. Data were reviewed by a single researcher.

Data-Gathering Tool

Information collected by the data-gathering tool consisted of demographic data; past history of disease activity as to American Rheumatism Association criteria; prepregnancy, pregnancy, and postpartum periods; medication being taken.

Prior to utilization of this tool, a pretest was performed. When the information obtained by the researcher was compared with that of another person the results were similar. In using the tool it was felt the information obtained was the minimum, basic information required.

Statistical Analysis

The data collected were examined in a descriptive approach. This method of analysis was felt to be most appropriate for this study because of the severe limitation of sample size, sole utilization of medical records for data collection, the retrospective nature of the study, and the severe limitations of the uncontrolled variables.

Limitations

In addition to the limitations described in Chapter 1 the following limitations became apparent as the study progressed:

1. No uniform point was set for beginning data collection in relation to disease process, diagnosis, or delivery.

2. The length of time over which survey data were available did not compare between groups, one week shortest time and six years, four

months longest. In all but one of the pregnant group only months were surveyed. Thus, comparisons between the group of patients who were pregnant and those who had never been pregnant were not possible although originally intended.

3. The two groups were not adequately matched. This may have been due in part to the vague criteria for grading disease activity used in this study.

Chapter 4

PRESENTATION OF FINDINGS

The major purpose of this study was to discover whether or not pregnancy precipitated exacerbation of disease activity in six women with diagnosed SLE. The two subsidiary purposes were to find out (1) whether there is a difference in the occurrence of exacerbations of SLE during the first, second, and third trimesters of pregnancy and (2) whether there is a difference in the occurrence of exacerbations during prepregnancy, pregnancy, and the postpartum periods of the SLE patient.

Descriptive Data

Demographic Data

The sample of 12 women with SLE consisted of six women who had never been pregnant and six who became pregnant between the time the original diagnosis was made and the time of the survey. The racial characteristics were similar in each group; the total group consisted of four Caucasians, six Mexican-Americans, and two Blacks. Ages ranged from 18 through 29. The two groups were matched on age, plus or minus five years; presence or absence of corticosteroid administration; grade of disease activity. The period prior to the surveyed pregnancy for Group A and prior to exacerbation for Group B was used for comparison. Because of the multiple exacerbations in all but two cases in Group B, the first stable time after the first recorded exacerbation was used for reference. Table 1 compares these data.

Table 1

Comparison of Pregnant and Nonpregnant Groups According to Age, Grade of Disease Activity, Presence or Absence of Cortiocosteroid Administration

Pregnant				Nonpregnant			
Patient	Age	Steroid	Grade	Patient	Age	Steroid	Grade
A	20	Present	II	J	22	Present	II
B	18	Present	I	I	21	Present	I
C	27	Present	I	H	29	Present	I
D	29	Absent	I	G	27	Absent	I
E	27	Present	I	K	26	Present	I
F	21	Absent	0	L	25	Absent	0

Case Studies of Pregnant Group

In the sample of six pregnant women there was a total of eight pregnancies. Table 2 summarizes the reproductive history prior to the surveyed pregnancies.

Case A. At age 16, this Caucasian female first had symptoms of SLE, which included migratory arthralgias, afternoon and evening fevers, bilateral subcostal pain, and blotchy skin eruptions over the cheek bones. The ANA and LE cell tests were positive, each on three occasions. The sedimentation rate was elevated but the creatinine clearance and VDRL were normal. Symptoms were controlled with 20 to 40 mg of prednisone daily, although symptoms recurred with attempts to reduce the dosage.

One month after this initial diagnosis she was rehospitalized for fever, pleuritic chest pain, and blood cultures positive for alpha streptococcus. Treatment included antibiotics, Imuran 75 mg daily and large doses of prednisone from 60 to 120 mg daily. After one month she was discharged on 45 mg of prednisone and 75 mg of Imuran daily. She continued to take these medications over the next two and one-half years, although the prednisone was slowly reduced despite episodic arthralgias, pleuritic pain, and myalgias. During this time she married and became pregnant for the first time, despite an intrauterine device. She chose to continue the pregnancy regardless of medical advice, and the Imuran was subsequently reduced at five months and discontinued at seven months. At 34 and 36 weeks gestation she went into labor prematurely and delivered a male child weighing 5 pounds, 5 ounces with no anomalies, but an apgar

Table 2

Reproductive History Prior to Surveyed Pregnancy

Patient	Gravida	Term	Premature	Abortion	Living Children
A-1	0				
A-2	2		1		0
A-3	2	1	1		1
B	0				
C	6	1	1	4	1
D	5	4		1	4
E	0				
F	0				

of 1/7. The child died three days after birth. The exact cause of death was unknown. No postmortem examination results were recorded on the chart.

No symptoms of exacerbation were noted during the pregnancy, delivery, or postpartum except for stiffness of joints, fever, and malaise several days prior to delivery. While in labor and the immediate postpartum period she received 100 mg of Solu-cortef, two 100 mg doses of cortisone acetate, and two 20 mg doses of prednisone.

One week following discharge the prednisone was tapered off with no flare of symptoms. Five months after delivery she was working part-time, asymptomatic, and off all medication, and ANA and LE cell tests were negative.

At age 20, during this asymptomatic period, she became pregnant for the second time. She remained asymptomatic through the pregnancy and delivered a full-term male child weighing 7 pounds, 6 ounces, with an apgar of 9/10; no anomalies were noted. No medication was given during labor or postpartum, and she remained symptom free.

She became pregnant for the third time at age 22. During pregnancy and delivery no manifestations of disease activity were noted, and she delivered a full-term female weighing 7 pounds, 11 ounces with an apgar of 9/10. Six weeks postpartum she noted the onset of joint stiffness, which was successfully controlled with aspirin. No other clinical manifestations of disease activity were noted at this time; her sedimentation rate was normal, the ANA was positive. Three months later joint pains continued, but no other symptoms occurred.

Case B. At age 16, this Mexican-American female was diagnosed as having SLE. Clinical manifestations included hemolytic anemia, Coombs positive, a negative LE cell test, a false-positive VDRL and a positive ANA, arthralgias. Eight months later she became pregnant for the first time. Hemolytic anemia persisted during pregnancy, for which she received 10 mg of prednisone daily until the week before delivery, when it was increased to 15 mg because of a drop in hemoglobin. During the last trimester she had 1+ to 2+ edema, a trace of albumin in the urine a week prior to delivery, and a normal blood pressure. While in labor she had a grand mal seizure. Her blood pressure was 148/100 and there was a trace of urine protein and little edema. It was questioned whether the seizure was related to toxemia of pregnancy or to SLE. Treatment included magnesium sulfate, Dilantin, Aldomet, phenobarbital, and high dose corticosteroids: one dose of 100 mg of Solu-cortef, two doses of 50 mg Depo-medrol, and 20 to 40 mg of prednisone daily. Prior to delivery she also developed gross hematuria with urinalysis negative for bacteria. Within ten days the red blood cell count in the urine dropped from 250 to 50 and then to 3 prior to discharge. Areas of erythema were also noted about the knees.

A spinal and mid-forceps delivery was necessary because of a secondary arrest of labor. A viable male child was delivered weighing 8 pounds, 5 ounces at 37 weeks gestation with an apgar score of 3/7. No anomalies were noted. Blood loss during delivery was estimated at 1200 ml due to secondary uterine dystocia. Treatment included two units of blood and plasmanate.

During the postpartum period hospitalization was extended because of extreme lethargy, fevers, subcostal chest pain, a low hemoglobin, for which she received more blood, and a high bacteria count in the urine. Laboratory findings included a positive ANA and false-positive VDRL; elevated white blood count; negative LE cell test; 1.3 gm protein in a 24-hour urine test, and hemoglobin ranging from 7.6 to 8.3 gm. Her serum creatinine was normal, the reticulocyte count 12.5. At discharge she was feeling well, afebrile, and taking 20 mg prednisone daily. During the next three months she felt well but had episodic joint pains and a pale maalar rash; prednisone was reduced to 15 mg daily. Seven months after delivery she had a voluntary laparoscopic tubal sterilization.

Case C. This Mexican-American female was first diagnosed as having SLE at the age of 15, reportedly because of swelling of her knee and ankle and a false-positive VDRL. No treatment was prescribed until the age of 19, when she became pregnant, developed pneumonia, and was hospitalized for gross pulmonary hemorrhages. This hospitalization was complicated by a tracheostomy and a gastrectomy. Laboratory data at the time included false-positive VDRL, hemolytic anemia, Coombs positive, elevated sedimentation rate, ANA and complement within normal limits. She also had nephritis requiring dialysis for a time and underwent a kidney biopsy which showed diffuse proliferative glomerulonephritis.

By the age of 26 she became pregnant for the seventh time. Her reproductive history prior to this current pregnancy had included one full-term child, given away for adoption; one spontaneous abortion; three therapeutic abortions performed in anticipation of exacerbation, which

occurred anyway; and one premature delivery, stillborn. She had a strong desire to have a child, so with this seventh pregnancy medical help was not sought until after the fifth period was missed and abortion was out of the question. Throughout the pregnancy she remained on 17.5 mg of prednisone daily, plus Choledyl, Actifed, and vitamins. She had had a history of proteinuria, less than one gram per 24 hours, ever since her hospitalization at age 19. This proteinuria continued throughout the pregnancy with some untreated, mild hypertension. During the third trimester the creatine clearance dropped from 80 ml per minute to 50 ml per minute, while the serum blood urea nitrogen and creatinine remained normal. She was hospitalized at this time to assess renal function and because a B-scan showed the child to be 32 to 33 weeks gestation, although by dates it was 39 weeks. A repeat creatinine clearance was reported at 84 ml per minute. The following day she spontaneously went into labor and delivered a viable male child weighing 3 pounds, 15 ounces with an apgar of 7/9 and no anomalies. During labor and immediately postpartum her blood pressure was elevated, 140/100 to 130/120, and treated with Apresoline. During labor she was also given 50 mg of Solucortef in addition to her regular daily dose of 17.5 mg of prednisone. Laboratory results during delivery included false-positive VDRL, negative ANA, complement 3 normal, total complement and complement 4 below normal.

The day following delivery she had a voluntary tubal ligation. Three days later she was discharged on 17.5 mg of prednisone daily. Throughout pregnancy and delivery she had no clinical symptoms of disease activity aside from the laboratory data already mentioned.

The fourth day after discharge she began having manifestations of disease activity including fever and chills; malaise; unawareness of her surroundings; paroxysms of cough, which became progressively worse and caused dehisence of the incisional wound; vomiting; joint paint. She was readmitted 12 days after the previous discharge. Laboratory data at this time included false-positive VDRL, negative ANA, hemoglobin 7.4 gm, Coombs positive (2+ direct); Westergren sedimentation rate 146; anergy to skin tests; complement 3 normal. Treatment included 40 mg of Solumedrol and 45 to 60 mg of prednisone daily. She remained in the hospital only five days, leaving prematurely because there was no one to look after her child. At discharge a low-grade temperature and cough continued. She was discharged on 40 mg of prednisone. No follow-up visit is recorded.

Case D. At age 24 this Mexican-American female was diagnosed as having SLE with initial major symptoms involving Raynaud's phenomenon of the hands. Symptoms were successfully treated with corticosteroids and dibenzyline regimen. Two years later, one month after the birth of her fifth child, she was rehospitalized with fever, migratory arthralgias, night sweats, subcostal chest pain, and anterior chest pain. Laboratory results at the time showed leukopenia, false-positive VDRL, and negative LE cell and ANA tests. The next year the Raynaud's phenomenon progressed, necessitating a right and left cervical sympathectomy.

At the age of 29 she became pregnant for the sixth time. Reproductive history included four full-term deliveries and one spontaneous abortion. During pregnancy no corticosteroids were taken, only iron and vitamins. She was asymptomatic until approximately two weeks prior to

delivery, when she complained of chest pain and the hemoglobin dropped to 10.3. At 39 weeks gestation she delivered a 6 pound, 7 ounce female with an apgar of 7/8. First-stage labor was complicated by meconium stain. Two days following delivery she had an elective tubal ligation. Hemoglobin remained low, 9.2, at discharge. No other symptoms were noted.

An isolated clinical entry one year later stated that Raynaud's had progressed, involving the legs bilaterally. She was limited to walking only two blocks before severe pain occurred. Laboratory data included a positive ANA test, a negative LE cell, and positive rheumatoid factor 1:10.

Case E. This 26-year-old Mexican American had one prenatal visit, at approximately five months gestation, prior to delivery of a viable 4-pound, 4½-ounce female with an apgar of 7/9. Estimated date of conception was unknown, but the child was considered premature.

Disease activity dated back nine years, when diagnosis of rheumatoid arthritis had been made and treatment of salicylates and gold therapy instituted. Approximately one year prior to pregnancy she had an acute flare of disease activity, was hospitalized, and diagnosed as having SLE.

Major clinical symptoms included neuropathy and myopathy. Medications taken during pregnancy included 25 mg of prednisone twice daily, Dilantin, vitamins, and iron. On the delivery day and first postpartum day the dosage of prednisone was increased to 80 mg, then reduced to 40 mg at discharge. Laboratory results at the time of delivery included normal complement 3, ANA, VDRL, and hemoglobin. During the three-day hospitalization she remained asymptomatic. No follow-up record was available.

Case F. For this Caucasian female diagnosis of SLE was made at age 14 with initial symptoms including butterfly rash, edema associated with renal disease, and blood tests (records not available). She had had no prescribed treatment and had remained asymptomatic except for a butterfly rash.

She became pregnant for the first time at age 20. Prior to delivery she had one prenatal visit at approximately two months gestation. At an estimated 5½ to 6 months gestation she began feeling tired with progressive weakness and dizziness, plus shortness of breath on exertion. This progressed over several weeks until after she had suffered with fevers to 104° and alterations in consciousness her family had her admitted to the hospital. One week prior to admission was the last time she reported fetal motion. On admission the laboratory tests yielded the following results: hemoglobin 4 gms; positive Coombs test, both direct and indirect measurements; false-positive VDRL; and positive ANA and LE cell. She was transfused with six units of packed red blood cells and begun on Decadron, totaling 24 mg in 24 hours, and thereafter 60 mg of prednisone daily. She improved symptomatically but signed out of the hospital against medical advice because of financial problems. She was readmitted at another institution. By dates she was approximately 31 weeks gestation but only 18 weeks by size. After three days she spontaneously delivered a macerated male fetus with no external malformations but with extensive placental infarction.

Two days prior to delivery the prednisone was discontinued. Laboratory data at the second institution included negative Coombs and

ANA tests, and a false-positive VDRL. The day following delivery she was asymptomatic and therefore discharged. No further record was available.

A summary of fetal outcome is presented in Table 3. A summary of the number of exacerbations occurring during the first, second, and third trimesters is presented in Table 4. In Case F the determination of the occurrence of exacerbations is questionable since this patient was reported to be 31 weeks by gestation but only 18 weeks by size. Table 5 summarizes the number of exacerbations occurring in the pre-pregnancy, pregnancy, and postpartum periods. In Case B it is assumed the exacerbation occurred prior to delivery and continued into the postpartum.

Case Studies of Nonpregnant Group

Case G. At the age of 23 this Black female was first diagnosed as having SLE. Initial manifestations included fever, precordial chest pain, myalgia, arthralgia, fatigue, anorexia with weight loss. Laboratory data showed a marked elevation in the sedimentation rate, a negative VDRL, a positive ANA, no LE cells in three samples, hypergammaglobulinemia, rheumatoid factor 1:640, 24-hour urine protein of 520 mg. Symptoms were treated with salicylates, 12 tablets daily. After discharge the joint pains continued and some dyspnea was noted on exertion. Thirteen days after discharge she was readmitted with high fever and chest pain that was worse on inspiration and lying down. Chest x-ray showed an enlarging heart and mild diffuse infiltrates on the lungs bilaterally. Hemoglobin

Table 3

Fetal Outcome

Patient	Sex of Child	Weeks Gestation	Birth Weight	Apgar	Demise	Anomalies
A-1	M	34-35	5- 5	1/ 7	x	
A-2	M	42	7- 6	9/10		
A-3	F	42	7-11	9/10		
B	M	37	8- 5	3/ 7		
C	M	32-33	3-15	7/ 9		
D	F	39	6- 7	7/ 8		
E	F	Unknown	4- 4	7/ 9		
F	F	31	--	--	x	

Table 4

Summary of Exacerbations During Pregnancy According to Trimester

Patient	Trimester		
	First	Second	Third
A-1			
A-2			
A-3			
B			x
C			
D			
E			
F			x

Table 5

Summary of Exacerbations According to Prepregnancy, Pregnancy, and Postpartum Periods

Patient	Prepregnancy	Pregnancy	Postpartum
A-1			
A-2			
A-3			x
B		x	
C			x
D			
E			
F		x	

was 7.7 gm, sedimentation rate was 59. She was started on 60 mg of prednisone daily with rapid improvement of symptoms.

Clinical records were available for the next seven months. During this time she was asymptomatic except for an occasional report of chest pain; prednisone was slowly tapered to 10 mg every other day. For the next three years she received medical care at another institution, receiving varying dosages of prednisone and being admitted to a hospital once for pancreatitis.

On return to the clinic she reported taking 5 mg of prednisone every one or two weeks, depending on her symptoms. At this time all prednisone was discontinued. During the next 15 months she experienced episodes of chest pain which were partially controlled by Ascriptin. At the end of this time she was admitted again for chest pain, fever, and arthralgias. Antinuclear antibody was 4+ at 1:16 dilution, sedimentation rate 46, total complement low; echocardiogram showed no evidence of pericarditis. The treatment included 500 mg and 250 mg of Solu-medrol followed by 60 mg of prednisone daily, tapered to 40 mg daily at discharge, and Arthropan.

Chest pain waxed and waned during the next several months, with prednisone dosage ranging from 10 to 45 mg daily. Six months after the last discharge she was admitted again with arthralgia, fatigue, alopecia, pruritic macular rash, and subcostal and precordial chest pain. Treatment consisted of 80 mg of prednisone tapered to 40 mg at discharge plus Arthropan. Two weeks after discharge she was readmitted with changes in mentation and incoherent speech. Temperature was 103° F, axillary; the

sedimentation rate, 66; blood urea nitrogen, 40; urinalysis granular and hyaline casts; no urine output since admission. She was given 1 gm of Solumedrol for three consecutive days. On the third hospital day she developed a respiratory arrest and was intubated; a cardiac arrest followed and she expired.

Case H. At age 27 this Caucasian female first had symptoms of SLE with intermittent arthralgias, fever, fatigue and anemia. Six months later she was hospitalized for joint pains, fever and night sweats; a diagnosis of SLE was made. Laboratory results at the time yielded the following results: positive ANA and LE cell, rheumatoid factor 1:1280, low serum complement, hypergammaglubulinemia, slightly elevated blood urea nitrogen, creatinine clearance 53 ml per minute; leukopenia; and 24-hour urine protein 60 mg. It was felt she most likely had focal proliferative nephritis, not nephrotic. Treatment consisted of 40 mg of prednisone daily and Persistin, which rapidly relieved her symptoms.

Several weeks after discharge, while continuing to take 40 mg of prednisone daily, she began having a recurrence of symptoms, so the prednisone was increased to 80 mg every other day. The first day off the medication she became confused, weak, and febrile, and complained of leg pains. She was readmitted approximately one month after the previous discharge. During hospitalization she had a spiking of temperature to 103.8°F; pleuritic chest pain; spontaneous pneumothorax, chest tube placement; macular hemorrhage in the left eye, sealed with laser beam; oral ulcers; a paranoid reaction with depression; staph aureus coagulase positive septicemia; hemolytic anemia. Treatment included prednisone in

various dosages up to 100 mg daily and then decreased progressively to 30 mg daily at discharge.

One month after discharge she was readmitted for incision and drainage of an abscess in the buttocks from previous injection sites. She is an elementary school teacher and taught full time the next year. Clinical records during the next eight months state that she was doing well with 15 to 20 mg of prednisone daily, with only occasional joint pains.

Nine months after the last hospitalization for exacerbation she was readmitted with complaints of nausea, fever, night sweats, back and leg pains. She was found to have a urinary tract infection; ANA and LE cell were positive. The fourth day of hospitalization she signed out against medical advice on 30 mg of prednisone daily and promptly returned to work despite fever and urinary tract infection. One month after leaving the hospital she was readmitted with fever, arthralgia, intermittent pleuritic pains. Symptoms were treated with large doses of steroids up to 200 mg daily and tapered to 20 mg daily at discharge. Also 50 mg of Cytoxan daily was initiated. The ANA remained positive, creatinine clearance varied from 52 ml per minute to 87 ml per minute, LE cell was negative, and blood cultures positive for staph aureus coagulase. No further records were available.

Case 1. At the age of 20, this Mexican-American female was diagnosed as having SLE, primarily because of an erythematous rash, arthralgias, fever, and a positive ANA. During the next year she worked in a factory until she developed a rash involving the face, chest, and

abdomen, which was treated with 60 mg of prednisone daily. Three months later she was admitted to a hospital with a deterioration in mental status, violent behavior, disorientation, joint pains, headache, dizziness, and continued rash. The prednisone was reduced to 15-20 mg to rule out steroid psychosis. At this time all neurological testing was normal, but the sedimentation rate was elevated. Mentation gradually cleared on 15 mg of prednisone daily. Steroid challenge accentuated her psychosis, so it was felt to be primary in nature. She was transferred to a psychiatric unit, where she was stabilized on Haldol and Cogentin. Depression continued. She was discharged two months later on 15 mg of prednisone every other day.

Clinic records over the next year-and-a-half show she was stable on 20 to 30 mg of prednisone taken every other day. The ANA remained positive, complement low, sedimentation rate elevated. Episodic joint pains and nervousness continued. She was unable to do her regular work but did volunteer work.

Case J. This Mexican-American female had a history of seizures beginning at age 10. From 15 to age 21 she had no seizures, the episodes being well controlled on Mysoline. At age 21 she began having joint pains, fever, fatigue, diffuse hair loss, and malaise. These symptoms persisted, and six months later she was hospitalized. Clinical manifestations included blurred vision, which by history developed over the last two months, and was intermittent in nature; diplopia; mild headaches; shingles. Pertinent laboratory data included anti-DNA 12.8; positive ANA; sedimentation rate markedly elevated; urinalysis normal;

negative VDRL; anergy to skin tests; creatinine clearance 90 ml per minute. Renal biopsy showed lupus nephritis, focal in nature, with membranes spared. Ophthalmologic tests showed optic atrophy secondary to SLE because of the following symptoms: papilledema, visual fields consistent with increased blind spot, intermittent exotropia, mild proptosis. She was treated with Decadron for several days and then 120 mg of prednisone which was decreased to 80 mg daily at discharge.

During the next two months headaches, fever, blurred vision and tiredness continued. She was readmitted because of a seizure, chest pain, and flashing black and yellow lights in her eyes. Chest x-ray showed a small pleural effusion and an ultrasonic cardiogram, a small to moderate pericardial effusion. Prednisone was increased to 120 mg for four days and then decreased to 80 mg daily. Dilantin and phenobarbital were also initiated. During the next two months she improved although joint pains and rash continued; prednisone was reduced to 50 mg daily.

She was briefly readmitted after two months for gastroenteritis. After discharge her condition improved with a subsequent reduction in prednisone. Three months later while vacationing, her anticonvulsant medications were changed. One month later, after returning home, she was admitted with uncontrolled seizures. She was given a 100 mg dose of prednisone, which was tapered to 40 mg at discharge. Antinuclear antibody remained positive, creatinine clearance normal. Clinic records for the next two years showed disease activity fairly stable with occasional joint pains or rash. The major problem had been her loss of vision, which progressed until she is now legally blind. She does not work. Prednisone is maintained at 30 mg every other day.

Case K. At age 17 this Caucasian female was diagnosed as having SLE on the basis of a skin rash and joint pains. Treatment included 15 mg of prednisone daily, which she continued for eight years.

At 25 she was hospitalized for six days with fever and chest pain that increased on inspiration. During this time an ANA test was positive; VDRL negative; creatinine clearance normal; sedimentation rate slightly elevated. Treatment included 40 mg of Solu-medrol for three days, then 40 mg of prednisone daily. One month and a half after discharge she was readmitted with chest pain and hemoptysis. Chest x-ray and bronchoscopy at the time were normal. Treatment included 20 mg of prednisone daily.

During the next eight months, clinic records state, she was feeling well except for a stasis ulcer of the left leg and a relentless skin rash. She was once again hospitalized after eight months because of progression of the skin rash, mouth ulcers, chest pain, arthralgia, and night sweats. Antinuclear antibody remained positive, serum creatinine negative. Symptoms improved on 50 mg of prednisone, although the rash persisted.

Skin rashes continued during the next six months despite varying dosages of prednisone. She worked at two different jobs during this time. At the end of this six months she was hospitalized for three days with chest pains and a chronic productive cough. Two months later she was again briefly hospitalized with a skin rash, fever, pleuritic pain, and joint pains. Chest x-ray at this time was normal and ANA remained positive.

Clinical records for the following year showed continued problems

with recurring skin rash, and productive cough. Prednisone dosage varied from 20 to 60 mg daily.

Case L. At age 21 this Black female first had symptoms of SLE with a skin lesion on her left cheek which was biopsied and diagnosed as lupus. The lesion increased in size, and a generalized mildly pruritic rash occurred on both cheeks, forehead, dorsum of nose, arms, shoulders, and legs. The following year a kidney biopsy was performed which showed membranoproliferative diffuse glomerulonephritis. She was diagnosed as having SLE and started on 60 mg of prednisone daily, which was progressively tapered to zero over the next year. She appeared to have a fairly stable course throughout the next two years without any use of steroids. At the end of this time she had a flare of disease activity and was hospitalized with a rash, loss of hair, arthralgias, high fevers, malaise, weight loss, cough, and edema of the eyelids. A chest x-ray showed an enlarged heart and congestive heart failure with bilateral pleural effusions. Her course was complicated by two episodes of ventricular fibrillation, which was corrected by cardioversion and cardiac drugs. Laboratory data produced the following results: sedimentation rate markedly elevated, negative VDRL, 1.9 gm protein in a 24-hour urine test, creatinine clearance 52 ml per minute, positive ANA, normal anti-DNA, hypergammaglobulinemia. Dosages of prednisone during hospitalization ranged from 60 to 160 mg daily. Clinic notes after discharge showed gradual resolution of the pleural effusions and rash throughout the next month with a subsequent tapering of the prednisone to 30 mg daily.

Over the next seven months the patient had no symptoms, with

urinalysis normal, sedimentation rate dropping, creatinine clearance normal, the ANA remaining positive. Prednisone was slowly tapered to 12.5 mg daily.

Discussion

An exacerbation, as previously defined, is an increase of disease activity by one or more grades. A summary of disease activity over a period of time for the pregnant group and nonpregnant group is presented in Figures 1 and 2. These figures represent disease activity only for the length of time that documented medical records existed in each surveyed case, not for the past history which was also often available but without documentation. For example, the figure representing one week for Patient F is only for the actual medical document available, even though several weeks' history was also described in the record. Because of the brief medical records with resultant difficulty in grading disease activity or determining when clinical changes occurred, these figures are only estimates and should not be used as absolute representation of disease activity. They are given as a general summary of the case studies and should not be used in comparing the two groups.

Findings of the comparative study of the above case records indicate possible answers to the following questions:

Question 1. What effect will pregnancy have in precipitating exacerbation of disease activity in SLE women when they are compared with a similar group of SLE women not experiencing pregnancy? In a comparison of the number of exacerbations per group according to length of record,

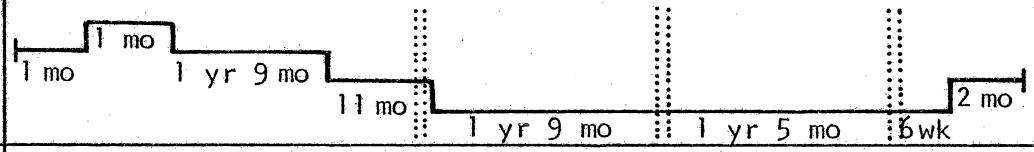
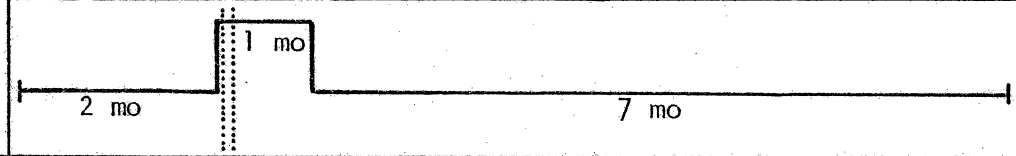
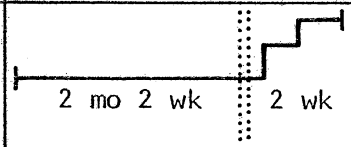
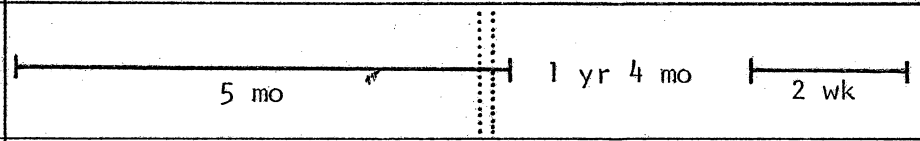
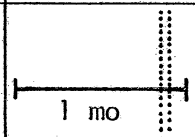
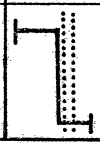
Patient	Grade	Disease Activity	Length of Record
A	3 2 1 0		6 yr 4 mo
B	3 2 1 0		10 mo
C	3 2 1 0		3 mo
D	3 2 1 0		5 mo 2 wk
E	3 2 1 0		1 mo
F	3 2- 1 0		1 wk

Figure 1

Summary of Disease Activity
for Pregnant Group

Delivery

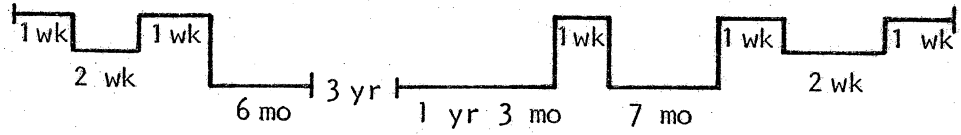
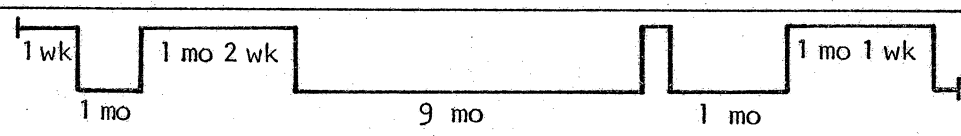
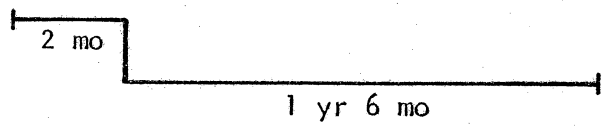
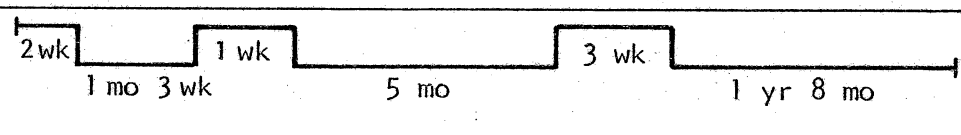
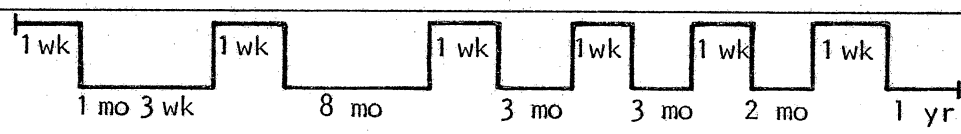
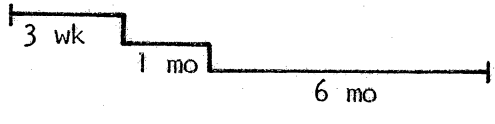
Patient	Grade	Disease Activity	Length of Record
G	3 2 1 0		2 yr 6 mo
H	3 2 1 0		1 yr 2 mo
I	3 2 1 0		1 yr 6 mo
J	3 2 1 0		2 yr 5 mo
K	3 2 1 0		2 yr 7 mo
L	3 2 1 0		7 mo 3 wk

Figure 2

Summary of Disease Activity for Nonpregnant Group

the nonpregnant group had more exacerbations over a period of time. This higher rate of exacerbation could be related to several factors. First, it should be noted that none of the nonpregnant group reached Grade 0 of disease activity, while two patients in the pregnant group were at this asymptomatic level. One questions if the two groups were equally matched according to disease activity. Failure to match could possibly be due to vague criteria for grading disease activity. Second, the only reason why the nonpregnant subjects were selected for the study was that they happened to be hospitalized because they were undergoing exacerbation of the disease. In comparison, only one of the pregnant group was admitted during a period of exacerbation. The rest were selected because they were pregnant and had SLE, but there was no correlation with exacerbation. A third factor was the length of medical record available per patient. In the pregnant group all but one medical record covered a time of less than 10 months whereas every case but one of the nonpregnant group covered at least one year and two months.

These data may be pointing to the fact that pregnancy does not always precipitate an exacerbation of disease activity, particularly in a well-controlled, stable prepregnancy state. Although four out of the eight pregnancies were associated with exacerbation, the small sample size makes the data inconclusive and generalization impossible.

Question 2. Is there a difference in the occurrence of exacerbations of SLE during the first, second, and third trimesters of pregnancy? The results showed no exacerbation during the first or second trimester and two exacerbations during the third trimester. Both of these

exacerbations occurred very close, within one month, to the time of delivery. In the reviewed literature Fraga, Zurier, and Estes similarly reported no exacerbations during the first trimester although all reported exacerbations during the second trimester (Fraga, and Others, 1974; Zurier, and Others, 1978; Estes and Larson, 1965).

Question 3. Is there a difference in the occurrence of exacerbations during the prepregnancy, pregnancy, and the postpartum periods of the SLE patient? The results showed exacerbation occurred equally between pregnancy and postpartum. Of four exacerbations, two occurred during the postpartum, two during pregnancy, and none during prepregnancy. All exacerbations occurred close to the time of delivery, two within one week of delivery and two within six weeks. It is difficult to generalize about these three periods, especially the postpartum, because of the short length of medical records available after delivery. Three case records ended within days of delivery.

The above data suggest exacerbation of disease activity occurs close to the time of delivery. Can this activation be related to an antigenic stimulus from fetal antigens occurring at or near the time of delivery? Can it possibly be due to a sudden suppression of 17-hydroxycorticosteroids at the termination of pregnancy? These questions must be answered by future research.

Chapter 5

SUMMARY, CONCLUSION, AND RECOMMENDATIONS

Summary

Systemic lupus erythematosus (SLE) occurs most frequently in women during the reproductive years. A review of the literature raised some question about the safety of pregnancy for women in this age group. It showed that exacerbation is a frequent occurrence postpartum and also reported a large number of cases where initial onset of SLE occurred during pregnancy. The conclusions reported in the literature, however, are subject to question for three reasons: no distinction was made in earlier studies between discoid lupus and SLE, no control groups were used, and the sampling was small.

This descriptive case study used medical records of six pregnant and six nonpregnant women with SLE. It was initiated to investigate the effect pregnancy would have in precipitating exacerbation of the disease activity when compared with those in a similar nonpregnant group. The difference in occurrence of exacerbation between the three trimesters of pregnancy and the prepregnancy, pregnancy, and postpartum period was also studied.

It was theorized that the reported increase in exacerbation could be related to a new antigenic stimulus provided in the form of fetal antigens to an already imbalanced maternal immune system. The mixing of fetal and maternal blood at the time of delivery, it was surmised, could

provide the mechanism for an outpouring of such antigens. A second theory was related to the abrupt suppression of 17-hydroxycorticosteroids at the termination of pregnancy, with a withdrawal of a possibly strong immunosuppressive mechanism active during pregnancy.

In a comparison of the number of exacerbations per group according to length of record, the nonpregnant group had more exacerbations. In the pregnant group, the only exacerbations occurred during the third trimester. In the prepregnancy, pregnancy, and postpartum periods there were two exacerbations in the postpartum period, two during pregnancy, and none during prepregnancy.

Conclusions

When a group of six pregnant women with SLE were compared with a similar group of nonpregnant SLE women, the occurrence of exacerbation was higher in the nonpregnant group. This may point to the fact that pregnancy does not always precipitate an exacerbation of disease activity. But because of the limitations of uncontrolled variables, low sample size, difficulty in matching disease activity and length of time since original diagnosis, and imbalance in length of hospital records, generalization of this finding is impossible. It does illuminate the problems of the study design and provide feedback for needed changes which will be discussed in the section on recommendations.

During the eight pregnancies reported, exacerbations occurred only during the third trimester, close to the time of delivery. It was also found that of the prepregnancy, pregnancy, and postpartum periods,

two exacerbations occurred during postpartum, two during pregnancy, and none during prepregnancy. These data suggest that if pregnancy is undertaken by women with SLE the risk of exacerbation might be greatest during the third trimester and postpartum. The sample size of the present study, however, is too small to make such a generalization.

This information would be helpful to the nurse in two respects. First, she could inform a questioning SLE woman that exacerbation of disease activity during pregnancy is not always the rule and that if exacerbation should occur, the limited data indicate it would most likely be during the third trimester, possibly close to the time of delivery, or postpartum. Secondly, the nurse caring for the pregnant or postpartum SLE woman could be cognizant that such minor complaints as joint pains, sore muscles, mouth ulcers, slight chest pain on inspiration, or unexplained low fever could possibly be heralding the onset of exacerbation.

Recommendations

In the future if a study similar to this is initiated it is suggested that instead of grading disease activity by the number of manifestations present, activity could be judged solely according to limitation. The following is a suggestive scale:

Grade 0: No limitation of activity, work or school

Grade 1: Partial limitation, possibly working

Grade 2: Limitation of activity, no work

Grade 3: Hospitalization

Also, continued contact with patients past the hospital setting and over

a longer period of time would provide more complete data about the various pregnancy periods.

As a further means to illuminate the relationship of SLE to the two theoretical bases for exacerbation, the following hypotheses are suggested:

1. Increasing parity in the SLE woman will have no significant (α=.05) effect on the number of exacerbations occurring during the pregnancy and postpartum periods.

2. There will be no significant (α=.05) difference between the time of delivery and exacerbation when a group of primiparous SLE women are compared to a similar group of multiparous SLE women.

3. During the monthly menstrual cycle of an SLE woman there will be no significant (α=.05) difference in clinical symptoms of disease activity during the time of menstrual flow or three days prior when compared with the fifteenth day of the cycle.

4. A prospective comparison of pregnant SLE patients will yield no consistent characteristics or factors present in those who do compared with those who do not have exacerbations.

SELECTED BIBLIOGRAPHY

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Bear, R. Pregnancy and lupus nephritis: A detailed report of six cases with a review of the literature. Obstetrics and Gynecology 47(6): 715-718, June 1976.

Beeson, P. B., and Others. Cecil: Textbook of Medicine. Philadelphia, W. B. Saunders Co., 1979.

Brien, T. G. and Dalrymple, I. J. Longitudinal study of the free cortisol index in pregnancy. Journal of Obstetrics and Gynecology 83(5): 361-367, May 1976.

Bulmash, J. M. Systemic lupus erythematosus and pregnancy. Obstetrics and Gynecology Annual 7:153-194, 1978.

Doe, R. P., and Others. Elevated nonprotein-bound cortisol in pregnancy, during estrogen administration and in carcinoma of the prostate. Journal of Clinical Endocrinology and Metabolism 29(6):757-766, June 1969.

Donaldson, L. B. and deAlvarex, R. R. Further observation on lupus erythematosus associated with pregnancy. American Journal of Obstetrics and Gynecology 83(11):1461-1471, 1 June 1962.

Estes, D. and Larson, D. L. Systemic lupus erythematosus and pregnancy. Clinical Obstetrics and Gynecology 9(2):307-321, June 1965.

Fessel, J. Systemic lupus erythematosus in the community. Archives of Internal Medicine 134(6):1027-1034, December 1974.

Fraga, A., and Others. Sterility and fertility rates, fetal wastage and maternal morbidity in systemic lupus erythematosus. The Journal of Rheumatology 1(3):293-298, September 1974.

Friedman, E. A. and Rutherford, J. W. Pregnancy and lupus erythematosus. Obstetrics and Gynecology 8(5):601-610, November 1956.

Galvao-Teles, A. and Burk, C. W. Cortisol levels in toxemic and normal pregnancy. Lancet 1(7806):737-740, 7 April 1973.

Garsenstein, M., and Others. Systemic lupus erythematosus and pregnancy. The New England Journal of Medicine 267(4):165-169, 26 July 1962.

Gemzell, C. Blood levels of 17-hydroxycorticosteroids in normal pregnancy. Journal of Clinical Endocrinology and Metabolism 13(8):898-902, August 1953.

Harris, R. E. and Lordon, R. E. The association of maternal lymphocytotoxic antibodies with obstetric complications. Obstetrics and Gynecology 48(3):302-304, September 1976.

Krakauer, R. S., and Others. Prevention of autoimmunity in experimental lupus erythematosus by soluble immune response suppressor. Science 1(3):293-298, September 1974.

McGee, C. D. and Makowski, E. L. Systemic lupus erythematosus in pregnancy. American Journal of Obstetrics and Gynecology 107(7):1008-1012, 1 August 1970.

Pence, H., and Others. Suppression of maternal responsiveness to paternal antigens by maternal plasma. Journal of Immunology 114(1):525-528, January 1975.

Rocklin, R. E., and Others. Effect of multiparity on human maternal hypersensitivity to fetal antigens. Nature 241(5384):130-131, 12 January 1973.

Rodman, G. P., Ed. Primer on the Rheumatic Diseases. New York, The Arthritis Foundation, 1973.

Terasaki, P. I., and Others. Maternal-fetal incompatibility. Transplantation 9(6):538-543, June 1970.

Thlikainen, A., and Others. Fetal leukocytes in the maternal circulation after delivery. Transplantation 17(4):355-358, April 1974.

Urman, J. D. and Rothfield, N. F. Corticosteroid treatment in systemic lupus erythematosus. Journal of American Medical Association 238(21): 2272-2276, 21 November 1977.

Vaughan, V. C., and Others. Textbook of Pediatrics. Philadelphia, W. B. Saunders Co., 1975.

Willson, J. R., and Others. Obstetrics and Gynecology. 5th ed. St. Louis, C. V. Mosby Co., 1975.

Zurier, R. B., and Others. Systemic lupus erythematosus: Management during pregnancy. Obstetrics and Gynecology 51(2):178-180, July 1977.

APPENDIX A

LETTER TO THE DIRECTOR OF MEDICAL RECORDS REQUESTING PERMISSION TO CONDUCT STUDY

Mrs. Marilynn Opincar, R.R.A.
Director of Medical Records
Loma Linda University Medical Center
Loma Linda, CA 92373

Dear Mrs. Opincar:

As a graduate student in nursing, I am investigating the effects of pregnancy on systemic lupus erythematosus. This study is to meet part of the requirements for a master's degree in nursing at Loma Linda University. I am hereby requesting permission to include medical records from Loma Linda University in my study. My committee chairman, Evelyn L. Elwell, has approved this thesis and I will obtain approval from the University Committee on Human Studies.

The proposed research is a matched case contol study of retrospective design utilizing medical records. Medical records will be reviewed from the years 1968-1978 and all patients who meet the sample criteria will be included. Data will be extracted from the records utilizing a data extraction checklist for each patient. All data will be collected under a code number by a single researcher. Names with assigned code numbers will be kept on a separate listing to be destroyed.

With your permission I would like to begin data collection during the first week in May. I expect to collect data on at least eight patients in a period of three to four weeks. I will be happy to make an appointment with you to discuss this research further if you desire. Space has been provided on the attached letter from the Graduate Program for your reply. Thank you for your assistance.

Sincerely,

Julia Christensen

Julia Christensen, R.N., B.S.
Graduate Program in Nursing
Loma Linda University
School of Nursing

CONSENT FORM

As a graduate student in nursing and as part of the requirements for a master's degree in nursing, I am investigating the effects of pregnancy on systemic lupus erythematosus. Medical records will be examined primarily to ascertain the possibility of pregnancy causing exacerbation of disease activity.

I am hereby requesting permission to include Loma Linda University's medical records in this study, which is explained in more detail below. Patients will not be contacted or asked to sign a consent form.

Criteria For Sample Selection

1. Female.
2. Age 16 through 45.
3. Systemic lupus erythematosus diagnosed according to ARA criteria.
4. Documented history of pregnancy past the 16-week gestation (group A, required of 4 patients).
5. No history of pregnancy (group B, required of 4 patients).
6. Diagnosis of lupus prior to pregnancy.

Procedure

Medical records will be reviewed from the years

1968-1978 and all patients who meet the sample criteria for group A will be included in the sample. The records will then be surveyed for all who meet the criteria for group B. Group B will then be matched to group A. Data will be extracted from the records utilizing a data extraction checklist for each patient. All data will be collected under a code number by a single researcher. Names with assigned code numbers will be kept on a separate listing to be destroyed. Risk for the patient either physically, emotionally, or socially is minimal, only occurring through a breach of confidentiality, which will be carefully guarded.

Julie Christensen — April 27, 1979

Graduate Student — Date

Evelyn L. Elwell

Guidance Committee Chairman — Date

APPENDIX B

LETTER FROM ETHICS IN STUDENT RESEARCH COMMITTEE REFERRING STUDY TO UNIVERSITY COMMITTEE ON HUMAN STUDIES

LOMA LINDA UNIVERSITY

Loma Linda Campus
LOMA LINDA, CALIFORNIA 92350
La Sierra Campus
RIVERSIDE, CALIFORNIA 92515

SCHOOL OF NURSING

Approval Date April 17, 1979

Julia Christensen
854 Pine Avenue, Apt B
Redlands, CA 92373

Dear Graduate Student:

The Ethics in Student Research Committee has reviewed the proposal you submitted for a research study to partially fulfill the School of Nursing requirements for a Master of Science degree from Loma Linda University.

The Committee has voted that your study is:

____ Approved as submitted in the specified setting for one year.

____ Approved in the specified setting for one year after the recommended changes have been made and a memo from your research chairman to this effect has been received by the committee chairman.

____ Not approved as submitted to the committee. See the attached comments for recommended changes. Must be resubmitted prior to any data collection.

__x__ Deferred to: __x__ UCOHS ___ Research Chairman ___ Other

__x__ Please see attached recommendations and/or comments regarding this action.

Please remember to give all signed consent forms to the Research Coordinator. Please contact the Chairman of the Ethics in Student Research Committee if you have questions related to the decision of the Committee. If any changes are made in the hypothesis, tool, consent form, or the procedure for data collection, this proposal must be resubmitted to this Committee. If data collection extends beyond one year the proposal must be resubmitted to the Committee.

We pray that the Lord will continue to bless your endeavors.

Sincerely,

Evelyn L. Elwell

Evelyn L. Elwell, Chairman
Ethics in Student Research Committee

xc: Research Committee Chairman - Evelyn Elwell

RECOMMENDATIONS AND/OR COMMENTS

Get consent from Mr. Ruffcorn or his office for permission to review charts.

Comments: Is this study justifiable as a nursing study?

APPENDIX C

ADVISOR APPROVAL OF RESEARCH PROPOSAL SUBMITTED TO THE UNIVERSITY COMMITTEE ON HUMAN STUDIES

ADVISOR APPROVAL OF RESEARCH PROPOSAL SUBMITTED TO THE UNIVERSITY COMMITTEE ON HUMAN STUDIES

To: Dr. Gordon Rick, Chairman, University Committee on Human Studies

From: Evelyn L. Elwell, Research Advisor

Subject: Research proposal approval for submission to the University Committee on Human Studies

Graduate Student's (Investigator's) Name: Julia Christensen

Date: 5/2/79 Option: Thesis X Non-thesis ___ Pub. Paper ___

The proposed research of this graduate student is of sufficient X, more than sufficient ___, excellent ___ scientific merit for fulfillment of the requirements for graduate study. I have approved its submission to the University Committee on Human Studies as it is outlined in the attached condensed research proposal. In my opinion, the extent of the emotional, physical, and social risk to the persons to be included in the proposed sample is non-existent X, minimal ___, moderate ___, other ___ (please explain). The proposed research is expected to contribute to the human welfare, is within the capability of the student and is feasible to carry out within a reasonable time. Thank you.

Evelyn L Elwell

Signature of the Research Advisor

This study was deferred to Human Studies because it is a retrospective chart review for which the student is not obtaining patient consent. Most of patients are deceased and this study is epidemiological in nature.

APPENDIX D

LETTER FROM THE UNIVERSITY COMMITTEE ON HUMAN STUDIES GRANTING PERMISSION TO CONDUCT THE STUDY

LOMA LINDA UNIVERSITY

Loma Linda Campus
LOMA LINDA, CALIFORNIA 92350
La Sierra Campus
RIVERSIDE, CALIFORNIA 92515

GRANTS RESOURCES SERVICE

May 14, 1979

Julia Christensen
c/o Dr. Evelyn Elwell
School of Nursing
Loma Linda University

Dear Ms. Christensen:

Your proposal for a study entitled "The effect of pregnancy on systemic lupus erythematosus" was reviewed by the Committee on Human Studies of Loma Linda University at its regular meeting May 9, 1979.

The actions of the committee are as follows:

The subjects are not at risk.
The protocol is approved.

If there are modifications to the proposed research protocol or consent form, or problems arising from the study, please notify the committee in writing of these changes or problems. If you have questions, please feel free to contact us.

You will be asked to provide a progress report on this study in six months, or at the conclusion of this study.

Best wishes in your project.

Sincerely yours,

Linda G. Halstead

Linda G. Halstead
Secretary
Committee on Human Studies

LGH:ag
Enc

APPENDIX E

AMERICAN RHEUMATISM ASSOCIATION PRELIMINARY CRITERIA FOR CLASSIFICATION OF SLE

AMERICAN RHEUMATISM ASSOCIATION PRELIMINARY CRITERIA FOR CLASSIFICATION OF SLE

A patient is said to have SLE if any four or more of the following 14 manifestations are present either serially or simultaneously.

1. Facial erythema (butterfly rash)
2. Discoid lupus
3. Raynaud's phenomenon
4. Alopecia
5. Photosensitivity
6. Oral or nasopharyngeal ulceration
7. Arthritis without deformity
8. LE cells
9. Chronic false-positive STS
10. Proteinuria of greater than 3.5 g/day
11. Cellular casts
12. One or both of the following: (a) pleuritis, (b) pericarditis
13. One or both of the following: (a) psychosis, (b) convulsions
14. One or more of the following: (a) hemolytic anemia, (b) leukopenia, (c) thrombocytopenia (Bulmash, 1978, p. 171).

APPENDIX F

DATA EXTRACTION CHECKLIST

DATA EXTRACTION CHECKLIST

Patient Identification Data

Code Number	DOB	Race:	Caucasian Hispanic Asian Black American Indian Other
Date of LMP:	Para: Gravida:	Outcome of previous pregnancies:	
Date of Delivery:	Type of Delivery:	Fetal Outcome:	Viable Stillborn
Maternal Demise:		Cause of Death:	

ARA Criteria for Diagnosis

1. Erythematosus rash	8. Serosal inflammation	11. False positive STS
2. Discoid lupus	a. pleuritis	12. Proteinuria (3.5 gm)
3. Alopecia	b. pericarditis	13. Cellular Casts
4. Photosensitivity	9. CNS changes	14. Hematologic
5. Oral/nasal ulcers	a. psychosis	a. Anemia
6. Raynaud's Phenomenon	b. convulsions	b. Leukopenia
7. Arthritis/no deformity	10. False Positive STS	c. Thrombocyto

OTHER:

ABSTRACTED DATA:

	Pre Pregnancy	1st Tri	2nd Tri	3rd Tri	Post Partum	6 mo.
Manifestations of Exacerbations						
Steroids						
Other						

Brief Narrative Summary: