WOMEN'S INTERAGENCY HIV STUDY
SECTION 18: PREGNANCY PROTOCOL

THE PREGNANCY PROTOCOL WAS DISCONTINUED AT VISIT 23

A. STUDY PURPOSE

The goal of the WIHS Pregnancy Protocol is to investigate the influence of pregnancy on HIV-infected women and how pregnancy alters the natural history of HIV disease.

B. RESEARCH GOALS

Hypothesis 1: Pregnancy alters the natural history of HIV disease, starting in the first trimester.

Specific Aims:

1. Determine the change in viral load in women who get pregnant and in a matched group who do not.
2. Determine change in CD4 count in women who get pregnant and in a matched group who do not.
3. Determine change in clinical status in women who get pregnant and in a matched group who do not.
4. Determine the incident rate of resistant viral strains during pregnancy as compared to times when not pregnant.

Hypothesis 2: Pregnancy leads to an up-regulation of coincident infections and changes the consequences thereof.

Specific Aims:

1. Determine types and quantity of HPV (PCR alone vs. Hybrid capture and PCR) in CVL before and during pregnancy, compared to women who are followed for same length of time without pregnancy.
2. Compare cytologic and histologic changes associated with oncogenic HPV types outside pregnancy.

Hypothesis 3: High maternal viral load will correlate with early pregnancy wastage and perinatal transmission of other pathogens.

Specific Aims:

1. To measure HIV-1 viral load stored from visit preceding documented pregnancy.
2. To correlate HIV-1 viral load with rate of early pregnancy loss.

Hypothesis 4: Pregnancy is associated with increases in the quantities of HIV-RNA present in cervico-vaginal secretions. Lower genital tract RNA quantities parallel increasing levels of progesterone and estrogens during gestation, more so than do plasma levels.

Specific Aims:

1. To perform assays on CVL samples obtained during one scheduled prenatal WIHS visit and the first regularly scheduled postpartum visit.

1. To compare CVL RNA quantities with plasma results and CD4 cell counts.

C. BACKGROUND

Pregnancy is known to be a time of immune modulation and has been cited as an example of the sexual dimorphism of the immune response. Despite the general recognition of the potential for pregnancy to alter host responses, remarkably little work to date has succeeded in contrasting the experiences of pregnant and non-pregnant women in the HIV epidemic. To a large extent, that gap in knowledge can be attributed to the difficulty in recruiting women prior to pregnancy and then being able to monitor them throughout gestation. Almost all reports to date derive from cohorts recruited during pregnancy. Thus it is difficult to determine if changes between late pregnancy and the postpartum period should be attributed to restitution to the pre-pregnancy state or to ongoing pregnancy effects. It is not only HIV per se that might be modified by the dramatic physiologic and hormonal alterations of pregnancy; coincident viral infections such as HPV and CMV might be affected as well and have significant clinical consequences. Since the WIHS begins following women prior to conception, it has the potential to contribute to the continuing dialogue regarding pregnancy and immune modulation, particularly in the early stages of gestation.

D. PARTICIPANT ELIGIBILITY

The study will be implemented at all sites within the WIHS. The goal is to accrue all women who have delivered since their last WIHS core visit. A woman will be considered eligible for enrollment if, on form F23, she responds that she has delivered a live birth or stillbirth (B9a, B10a or B11a = 1 or 2) since her last study visit. A PRNOTI (Participation Notification) form should be completed for every woman eligible for enrollment into the protocol.

E. OVERVIEW OF ENROLLMENT

If it is determined during the course of a participant's WIHS core visit that she has delivered since her last WIHS core visit, she will be asked to participate in the Pregnancy Protocol. At this time, the Pregnancy Notification Form (PRNOTI) should be completed for all eligible women indicating whether or not the participant consents to enroll in the Pregnancy Protocol. Indicate on the PRNOTI if the participant is: 1) eligible and has agreed to enroll in the substudy; 2) eligible, but has declined to enroll; or 3) eligible, but did not enroll for another reason, e.g., participant died before signing the medical record release forms.

During enrollment, clinical staff will collect and record on the PRNOTI the following information to aid in abstraction:

- Prenatal care provider(s)
- Institution(s) where prenatal care received
- Date(s) on which prenatal care received
- Labor/delivery provider
- Labor/delivery institution
- Date of labor/delivery

Once a participant has consented to be enrolled into the Pregnancy Protocol, she will be asked to give written consent for the release of her OB/delivery medical records. The Pregnancy Protocol will collect data via chart review by a site-designated person with obstetrical expertise (OB designee).

The Pregnancy Protocol involves the completion of two forms: Pregnancy (PR01) and Postpartum (PR02) that will be completed by the OB designee (verified through medical record abstraction). Form PR01 will collect data specific to medical conditions that occur during the course of pregnancy;

the covariates needed to evaluate the influence of pregnancy on HIV disease are not obtained during the core interview. Form PR02 will collect data on intrapartum complications, labs and medications; labor and delivery; postpartum history and complications; and medications on discharge.

F. MEDICAL RECORD ABSTRACTION

A copy of the completed PRNOTI form will be given to the site abstractionist/OB designee. Medical Record Abstraction will be done by the OB designee to complete the information collected on PR01 and PR02. At each WIHS site, a designee with obstetrical expertise (OB designee) will be appointed to assist with the completion of PR01 and PR02. Charts will be requested by each site's medical record abstractionist at least one month after the participant's reported delivery. Records may not be abstracted unless the participant has signed the corresponding medical record release form (site-specific).

Once received, the OB designee will review the delivery record and complete Forms PR01 and PR02 based on abstraction.

G. LABELING AND DATA ENTRY OF FORMS

All Pregnancy Protocol forms (including PRNOTI, PR01 and PR02) will be labeled with the core visit number at which the delivery participant's delivery was reported, i.e., the visit at which the participant was determined to be eligible for participation.

Site data entry staff will enter completed forms into Apollo.