ENDOMETRITIS

A MEDICAL DICTIONARY, BIBLIOGRAPHY,
AND ANNOTATED RESEARCH GUIDE TO
INTERNET REFERENCES

JAMES N. PARKER, M.D.
AND PHILIP M. PARKER, PH.D., EDITORS

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About the Editors

James N. Parker, M.D.

Dr. James N. Parker received his Bachelor of Science degree in Psychobiology from the University of California, Riverside and his M.D. from the University of California, San Diego. In addition to authoring numerous research publications, he has lectured at various academic institutions. Dr. Parker is the medical editor for health books by ICON Health Publications.

Philip M. Parker, Ph.D.

Philip M. Parker is the Eli Lilly Chair Professor of Innovation, Business and Society at INSEAD (Fontainebleau, France and Singapore). Dr. Parker has also been Professor at the University of California, San Diego and has taught courses at Harvard University, the Hong Kong University of Science and Technology, the Massachusetts Institute of Technology, Stanford University, and UCLA. Dr. Parker is the associate editor for ICON Health Publications.

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Table of Contents

FORWARD

In March 2001, the National Institutes of Health issued the following warning: "The number of Web sites offering health-related resources grows every day. Many sites provide valuable information, while others may have information that is unreliable or misleading."[1] Furthermore, because of the rapid increase in Internet-based information, many hours can be wasted searching, selecting, and printing. Since only the smallest fraction of information dealing with endometritis is indexed in search engines, such as **www.google.com** or others, a non-systematic approach to Internet research can be not only time consuming, but also incomplete. This book was created for medical professionals, students, and members of the general public who want to know as much as possible about endometritis, using the most advanced research tools available and spending the least amount of time doing so.

In addition to offering a structured and comprehensive bibliography, the pages that follow will tell you where and how to find reliable information covering virtually all topics related to endometritis, from the essentials to the most advanced areas of research. Public, academic, government, and peer-reviewed research studies are emphasized. Various abstracts are reproduced to give you some of the latest official information available to date on endometritis. Abundant guidance is given on how to obtain free-of-charge primary research results via the Internet. **While this book focuses on the field of medicine, when some sources provide access to non-medical information relating to endometritis, these are noted in the text.**

E-book and electronic versions of this book are fully interactive with each of the Internet sites mentioned (clicking on a hyperlink automatically opens your browser to the site indicated). If you are using the hard copy version of this book, you can access a cited Web site by typing the provided Web address directly into your Internet browser. You may find it useful to refer to synonyms or related terms when accessing these Internet databases. **NOTE:** At the time of publication, the Web addresses were functional. However, some links may fail due to URL address changes, which is a common occurrence on the Internet.

For readers unfamiliar with the Internet, detailed instructions are offered on how to access electronic resources. For readers unfamiliar with medical terminology, a comprehensive glossary is provided. For readers without access to Internet resources, a directory of medical libraries, that have or can locate references cited here, is given. We hope these resources will prove useful to the widest possible audience seeking information on endometritis.

The Editors

[1] From the NIH, National Cancer Institute (NCI): **http://www.cancer.gov/cancerinfo/ten-things-to-know**.

CHAPTER 1. STUDIES ON ENDOMETRITIS

Overview

In this chapter, we will show you how to locate peer-reviewed references and studies on endometritis.

Federally Funded Research on Endometritis

The U.S. Government supports a variety of research studies relating to endometritis. These studies are tracked by the Office of Extramural Research at the National Institutes of Health.[2] CRISP (Computerized Retrieval of Information on Scientific Projects) is a searchable database of federally funded biomedical research projects conducted at universities, hospitals, and other institutions.

Search the CRISP Web site at **http://crisp.cit.nih.gov/crisp/crisp_query.generate_screen**. You will have the option to perform targeted searches by various criteria, including geography, date, and topics related to endometritis.

For most of the studies, the agencies reporting into CRISP provide summaries or abstracts. As opposed to clinical trial research using patients, many federally funded studies use animals or simulated models to explore endometritis. The following is typical of the type of information found when searching the CRISP database for endometritis:

- **Project Title: BACTERIAL VAGINITIS AS A COFACTOR FOR HIV1 SHEDDING**

  Principal Investigator & Institution: Hitti, Jane E.; University of Washington Seattle, Wa 98195

  Timing: Fiscal Year 2001; Project Start 23-APR-2001; Project End 31-MAR-2006

  Summary: We propose a 5 year study of the interactions between reproductive tract infection, inflammation and genital HIV shedding in women. We plan to examine the

[2] Healthcare projects are funded by the National Institutes of Health (NIH), Substance Abuse and Mental Health Services (SAMHSA), Health Resources and Services Administration (HRSA), Food and Drug Administration (FDA), Centers for Disease Control and Prevention (CDCP), Agency for Healthcare Research and Quality (AHRQ), and Office of Assistant Secretary of Health (OASH).

hypothesis that increased genital tract HIV-1 shedding occurs in association with altered vaginal flora, cervicitis, and endometricitis, all of which are usually sub-clinical conditions that describes a continuum of ascending genital tract infection. An increase in vaginal and cervical proteolytic enzymes may promote the traffic microbes through the cervix to the endometrium to produce cervicitis and **endometritis.** The mechanisms by which abnormal vaginal flora, cervicitis increase genital HIV shedding include depletion of protective H2O2 lactobacilli, increased vaginal pH, decreased reduction-oxidation potential and altered vaginal and cervical inflammatory cytokines, which together selectively up-regulate LTR transcription through NF-kappaB. As such, oral antibiotic treatment of BV and cervicitis should decrease HIV shedding. We will examine the following specific aims: 1. To examine the associations between vaginal flora and HIV RNA concentrations in endocervical and vaginal fluid. We hypothesize that increased anaerobes, G. vaginalis and M. hominis in vaginal flora caused increased cervical and vaginal HIV RNA replication and that H2O2- producing Lactobacillus are productive. 2. To study the relationship between reproductive tract inflammation and genital HIV shedding. We hypothesize that an inflammatory response in the vagina, cervix and uterus results in increased genital HIV shedding. 3. To determine whether antibiotic treatment for bacterial vaginosis and cervicitis decreased genital HIV shedding. We hypothesize that oral antibiotic treatment will re-establish normal vaginal flora and decrease local inflammation, resulting in decreased endocervical HIV shedding. Women will be enrolled from 2 sites in the United States. In addition, a BV treatment study will be carried our in parallel in a cohort of HIV- infected Kenyan women not on anti-retroviral therapy. These studies should help to define the inter-relationships between altered vaginal flora, upper genital tract inflammation, the host inflammatory response and genital HIV shedding. By including an African cohort, we will learn about the relative contributions of genital tract infection and inflammation and anti-retroviral therapy to genital HIV load. Finally, we will learn whether antibiotic therapy with the goal to establish normal vaginal flora and decreases cervicitis and **endometritis** has the potential to decrease HIV shedding in the female genital tract in both anti-retroviral-experienced women and women without access to HIV treatment.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: CHLAMYDIA TRACHOMATIS ENVELOPE COMPONENTS AND VIRULENCE**

  Principal Investigator & Institution: Raulston, Jane E.; Pathology; East Tennessee State University Box 70565 Johnson City, Tn 37601

  Timing: Fiscal Year 2003; Project Start 30-SEP-2003; Project End 29-SEP-2004

  Summary: (provided by applicant): Chlamydia trachomatis is the leading bacterial agent of sexually transmitted infections in the United States and a major culprit in urethritis, cervicitis, **endometritis,** salpingitis, pelvic inflammatory disease, infertility and ectopic pregnancy. The highest chlamydial infection rates are observed in young people between 15 and 34 years of age. Throughout these peak reproductive years, the endometrial epithelial cell layer lining the uterine cavity is subject to constant changes in levels of micronutrients such as iron, due to hormonal cycling during menstruation. Endometrial epithelial cells are natural target host cells for infection by chlamydiae. The availability of iron is well-known to have a tremendous influence on the production of bacterial antigens, envelope components and virulence factors; these effects are particularly prominent for obligate intracellular pathogens such as chlamydiae. In other pathogens, virulence factors produced in response to low concentrations of iron elicit tissue damage in the host. Certain bacterial iron-regulated proteins are also

immunotherapeutic targets for vaccine design. In these studies, the mechanism for regulation of chlamydial iron-responsive proteins and antigens will be examined in Specific Aim 1. Specific Aims 2 and 3 will (i) determine the identities of chlamydial iron-regulated proteins, and (ii) quantitatively assess transcription of the genes encoding these components under iron-deficient growth conditions, respectively. In Specific Aim 4, an envelope transport system will be examined to determine whether or not it functions as a major iron-uptake pathway for the chlamydiae. The long-term objectives for these studies are to develop a better understanding of mechanisms for the destructive tissue pathology observed in chlamydial infections and to provide new insights on specific chlamydial proteins and antigens that could be tested for their immunotherapeutic potential.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: CHLORHEXIDINE IRRIGATION TO PREVENT INFECTION**

  Principal Investigator & Institution: Rouse, Dwight J.; Obstetrics and Gynecology; University of Alabama at Birmingham Uab Station Birmingham, Al 35294

  Timing: Fiscal Year 2001; Project Start 01-JAN-1999; Project End 31-DEC-2001

  Summary: Clinically overt infection of the placenta, fetal membranes, or uterus during labor (chorioamnionitis) complicates from 1% to 11% of pregnancies. The incidence of uterine infection after delivery (endometritis) varies from 1%-3% after vaginal delivery to 15-20% after cesarean delivery. Chorioamnionitis is a recognized risk factor for bacteremia and septic shock and is associated with a several-fold increase in the risk for cesarean delivery. Women who undergo cesarean delivery in the setting of chorioamnionitis are at increased risk of serious pelvic and wound infection. The most severe complications of **endometritis** (including, rarely, death from whelming sepsis) usually occur after cesarean delivery. The economic costs of chorioamnionitis and **endometritis** (collectively referred to as peripartal infection) are substantial and can be conservatively estimated at $120,000,000 a year in the U.S. for post- cesarean infections alone. The offspring of women with chorioamnionitis are exposed to invasive diagnostic testing (e.g. lumbar puncture for cerebrospinal fluid assessment), intravenous antibiotic therapy, prolonged hospitalization, sepsis, and death, Survivors face an increased risk of cerebral palsy. Furthermore, the costs of caring for infants born to mothers with chorioamnionitis may easily exceed the maternal costs of peripartal infection. Because the etiology of chorioaminonitis and **endometritis** is ascending infection of endogenous cervico-vaginal bacteria, intrapartum irrigation of the vagina and cervix with an anti-bacterial as a logical approach to prevention of peripartal infection. To be clinically useful, such an agent would need to possess broad antimicrobial activity, and be non-toxic and non-irritating for mother and fetus. Ideally the agent would be commercially available and inexpensive. The widely used medical disinfectant chlorhexidine satisfies these requirements. There we aim: 1) To conduct a placebo-controlled, double- masked, randomized clinical trial to determine whether intrapartum vaginal irrigation with a dilute chlorhexidine solution will prevent or lessen the trial to determine whether intrapartum vaginal irrigation with a dilute chlorhexidine solution will prevent or lessen the severity of the maternal peripartal infections--chorioamnionitis and **endometritis;** 2) To determine whether intrapartum vaginal irrigation with a dilute chlorhexidine solution will reduce the rate of microbial invasion of the chorioamnion; 3) To determine whether intrapartum vaginal irrigation with a dilute chlorhexidine solution will reduce the rate of acute histologic chorioamnionitis; 4) To determine whether the presence of bacterial vaginosis is associated with a differential effect of chlorhexidine vaginal irrigation on the maternal peripartal infection rate; and 5) To determine whether

intrapartum vaginal irrigation with a dilute chlorhexidine solution reduces the rates of neonatal sepsis.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: CLINICAL EPIDEMIOLOGY OF MYCOPLASMA GENITALIUM**

  Principal Investigator & Institution: Totten, Patricia A.; Professor; Medicine; University of Washington Seattle, Wa 98195

  Timing: Fiscal Year 2002; Project Start 01-MAR-2002; Project End 28-FEB-2007

  Summary: Large proportions of the major reproductive tract inflammatory syndromes remain idiopathic, not attributable to the major sexually transmitted pathogens such as Chlamydia trachomatis or Neisseria gonorrhoeae. Where effective STD control programs exist, most urethritis in men and endocervicitis or mucopurulent cervicitis (MPC) in women is no longer attributable to gonococcal or chlamydial infection. This is equally true for most upper genital tract complications of urethritis (epididymitis) or endocervicitis (endometritis, salpingitis and perinatal and puerperal morbidity). Mycoplasma genitalium, a fastidious bacterium discovered in 1981, now detectable by PCR, has been significantly associated with nongonococcal urethritis (NGU) in men in 11 of 11 studies over the past decade using PCR, including our own recent study which demonstrated M. genitalium in 27 (22%) of 211 men with and 5 (4%) of 117 without NGU (OR 6.5; 95% CI 2.1- 19.9). Recognition of M. genitalium as a pathogen in the male raises the important question of its role as a pathogen in the female, both in nonpregnant and in pregnant women. Since initial submission of this proposal in February 2000, we have completed two retrospective cross- sectional studies involving women. In a random sample of female STD clinic patients, we demonstrated endocervical M. genitalium infection in 24 (13%) of 191 with MPC vs. 27 (6%) of 453 without MPC (OR adjusted for cervical pathogens 3.0; 95% CI 1.6-5.8). This study also detected M. genitalium in 10 (14.3%) of 70 women with history of spontaneous miscarriage at < 20 weeks gestation vs. 41 (7.2%) of 570 without this history (adj OR=2.5; 95% CI 1.1-5.6). A cross-sectional study of 115 Kenyan women with suspected PID demonstrated M. genitalium in endometrial biopsies from 7 (12%) of 58 women with **endometritis** vs. 0 of 57 without **endometritis** (p=0.01). In our studies of male urethritis, MPC, and **endometritis,** associations of M. genitalium with disease were similar to, or stronger than, the associations with chlamydial infection. These data support our proposed studies as the next logical step in clinical epidemiologic studies of this pathogen. Our three specific aims are to (1) define the role of M. genitalium in acute salpingitis in women undergoing laparoscopy in Nairobi Kenya; (2) define the association of M. genitalium with abnormal pregnancy outcomes including preterm delivery of a low birthweight infant, using data and clinical specimens already available from 2500 women prospectively followed to term at University of Washington hospitals (including 625 with gestation <37 weeks); and (3) determine (a) risk factors for M. genitalium infection in a population-based sample of young women participating in Wave 3 of the National Longitudinal Study of Adolescent Health, and in a sample of higher risk women attending the Seattle STD clinic, and (b) concordance of M. genitalium infection in these women and their sex partners. M genitalium may represent an important new pathogen in the female reproductive tract. Studies of its association with salpingitis and pregnancy morbidity are essential. Future studies should also address whether, similar to gonorrhea and chlamydial infection, it facilitates transmission of HIV infection.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: DOUCHING, VAGINAL MICROBIOLOGY, AND PID**

  Principal Investigator & Institution: Ness, Roberta B.; Professor and Chair; Epidemiology; University of Pittsburgh at Pittsburgh 350 Thackeray Hall Pittsburgh, Pa 15260

  Timing: Fiscal Year 2001; Project Start 01-DEC-1998; Project End 30-NOV-2003

  Summary: Pelvic inflammatory disease is a major or cause of reproductive morbidity worldwide. Its sequelae include tubal infertility, chronic pelvic pain, recurrent PID and ectopic pregnancy. Douching is a common and possibly modifiable potential risk factor for PID, but a handful of previous studies examining this association are retrospective and conflicting. At the same time, compelling data suggest that douching may alter the vaginal microenvironment, thereby predisposing to bacterial vaginosis and perhaps, resultant PID, but this has not been fully tested. We propose to conduct a large, multicenter, prospective cohort study to examine the independent association between douching and PID and to study the effect of douching on vaginal microbiology. We will enroll 1800 women at high risk for acquiring sexually transmitted infections. Half will be women who report douching consistently at least once per month over the past six months; half will be women who report never douching in the past six months. Enrolled women will be evaluated at baseline by interview for behavioral characteristics related to douching and STD risk and by lower genital tract microbiology for N. gonorrhoea, C. trachomatis, bacterial vaginosis, and concentrations of lactobacillus, anaerobes and facultative bacteria. During 3-4.5 years of follow-up, serial interviews will be completed and self-obtained vaginal swabs assessed for lactobacilli and other vaginal bacteria. The primary outcome of PID (symptomatic endometritis), will be compared between the douching and non-douching groups. We will also compare the following: 1) gonococcal or chlamydial cervicitis at baseline, 2) bacterial vaginosis and semi-quantitative lactobacilli concentration at baseline, 3) change during follow-up in the concentration of lactobacilli (hydrogen-peroxide producing and non-producing), as well as anaerobic and facultative bacteria. Given the paucity of information regarding the relationship between douching and reproductive outcomes, the proposed study is imperative in order to direct future public health recommendations.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: HIV-1 SHEDDING FROM FEMALE GENITAL TRACT**

  Principal Investigator & Institution: Coombs, Robert W.; Associate Professor; Laboratory Medicine; University of Washington Seattle, Wa 98195

  Timing: Fiscal Year 2001; Project Start 23-APR-2001; Project End 31-MAR-2006

  Summary: This is a new Program Project application in response to RFA-HD-00- 006 to establish a Women's HIV Pathogenesis program at the University of Washington in collaboration the University of Rochester and the University of Nairobi, Kenya. The central Program these is to explore the hypothesis that the female genital tract is a separate virological compartment from blood. As such, viral application in the genital compartment may be influenced by several factors including the host's hormonal status (i.e., menses), and both viral and microbiological cofactors that could have an important influence on the evolution of HIV- 1 (i.e., generation of viral diversity), re-seeding of the blood compartment with potentially drug-resistant, and disease pathogenesis both within the genital tract (changes from favorable to unfavorable microbiological flora) and systemically (HIV-1 disease progression). Understanding these gender-specific HIV-1 factors may provide additional insight into the control of both vertical and horizontal transmission of HIV-1. To accomplish the central Program theme, we will use

three different cohorts of HIV-1-infected women recruited at the three collaborating institutions. The research activities of the Program Project will be accomplished through three Cores and three Research Projects. The infrastructure will reside within an Administrative Core (Core A) located at the University of Washington, a Clinical Core (Core B) and a Laboratory Core (Core C). Both internal and external advisory committees will review the Program's research progress and report to the Principal Investigator, Dr. Coombs. Since our hypothesis is that genital tract inflammation represents a continuum as defined by local vaginitis (bacterial vaginosis), to cervicitis (cytomegalovirus), to **endometritis** (microbial) and ultimately to pelvic inflammatory disease, each of the three research Projects are designed to capture this continuum. In Project I (HIV-1 shedding and evolution), we will characterize subjects for shedding of HIV-1, CMV and HSV-2, and definitively establish, through viral phylogenetic typing that HIV-1- re-emerges from the genital tract to re-infect the blood compartment in subjects that receive stable anti- retroviral therapy. In Project II (CMV co-shedding) we will show that CMV is an independent viral co-factor for HIV-1 shedding, whether CMV shedding from the cervix represents reactivation or re-infection, and that the suppression of CMV using valganciclovir can decrease HIV- 1 genital shedding. In Project III(Bacterial Vaginosis), we will show the effect of bacterial vaginosis as a local co-factor for HIV-1 shedding, how this local abnormal microbiological flora contributes to HIV-1 shedding through local cytokine-mediated mechanisms, and that anti-microbial treatment of bacterial vaginosis in both anti-retroviral treated and untreated women results in decreased HIV-1 genital shedding. Taken together, these studies will provide important comparative data to the male genital tract shedding of HIV-1 and may have implications for both the vertical and horizontal transmission of HIV-1.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: METRONIDAZOLE PLUS ERYTHROMYCIN TO PREVENT PRETERM BIRTH IN WOMEN**

  Principal Investigator & Institution: Caritis, Steve N.; University of Pittsburgh at Pittsburgh 350 Thackeray Hall Pittsburgh, Pa 15260

  Timing: Fiscal Year 2001

  Summary: Aims of the study are to 1)determine whether or not the administration of antimicrobial therapy in women with elevated cervical oncofetal fibronectin will reduce the risk of spontaneous preterm birth, reduce the risk of early neonatal sepsis, clinical chorioamnionitis, and early postpartum **endometritis,** and 2)determine the effect of antimicrobial therapy on fetal fibronectin positivity and its ability to prevent preterm delivery. Patients are screened at the time of a vaginal exam for the presence of cervical oncofetal fibronectin by obtaining two swabs. If the dipstick test for these swabs is positive, the specimen is sent to a central lab for an ELISA assay for the presence of fetal fibronectin. If the assay is positive, the patient is randomized into the double-blind, placebo-controlled trial of metronidazole 250mg vs. placebo/placebo. Patients take the study drug for 10 days and return for an exam similar to the screening exam.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: PREVENTION OF INFERTILITY IN WOMEN WITH SUBCLINICAL PID**

  Principal Investigator & Institution: Wiesenfeld, Harold C.; Magee-Women's Health Corporation 204 Craft Ave Pittsburgh, Pa 15213

  Timing: Fiscal Year 2003; Project Start 01-MAY-1998; Project End 31-JAN-2008

Summary: (provided by applicant): The broad, long-term goals of this study are to evaluate whether longer course antibiotic therapy for women at-risk for subclinical PID prevents subsequent infertility better than currently used short course antibiotic regimens for lower genital tract infections. Subclinical pelvic inflammatory disease (PID) is an important yet overlooked cause of infertility, responsible for more cases of post-infectious tubal infertility than acute PID. Subclinical PID is present in 25% of women with gonorrhea or chlamydia, and one in seven women with bacterial vaginosis, despite the absence of symptoms of acute PID. Most importantly, there is a doubling in infertility among women with subclinical PID compared to women without PID. Current treatment strategies for cervicitis and vaginitis do not address ongoing upper genital tract inflammation. Our hypothesis is that the preservation of fertility is greater among women with subclinical PID treated with a long-course antibiotic regimen compared to women receiving standard single-dose regimens for uncomplicated lower genital tract infections. The proposed application describes a randomized, double-blind, comparative phase III clinical trial studying a novel treatment regimen that incorporates azithromycin, an antimicrobial with potent immunomodulatory properties, on fertility outcomes in women at-risk for post-infectious fallopian tube damage. The specific aims are to 1) compare fertility rate of women with subclinical PID receiving two weeks of broad-spectrum antibiotic therapy with the fertility rate of women with subclinical PID receiving single-dose antibiotic regimen, 2) determine whether the resolution of **endometritis** is more common in women treated with the enhanced antimicrobial regimens utilized for acute PID compared to currently recommended single-dose regimens for lower genital tract infections, 3) characterize the inflammatory response in the lower genital tract in women with and without subclinical PID, and 4) evaluate whether women with subclinical PID have evidence of fallopian tube inflammation. During this study, very real public health questions will be asked and answered which will affect the way that lower genital tract infections are routinely managed, potentially enhancing fertility among American women.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: ROLE OF CYTOKINES AND PROMOTER GENOTYPE IN PREMATURITY**

  Principal Investigator & Institution: Krohn, Marijane A.; Associate Professor; Magee-Women's Health Corporation 204 Craft Ave Pittsburgh, Pa 15213

  Timing: Fiscal Year 2003; Project Start 14-APR-2003; Project End 31-MAR-2008

  Summary: (provided by applicant): Hypotheses: Decreased concentrations of pro-inflammatory cytokines in the lower genital tract early in pregnancy indicate a greater susceptibility to ascending microbial invasion. Increased cytokines in the cervix early in pregnancy indicate pre-existing ascending microbial invasion. African-American women are more likely to have extreme concentrations (lower or higher) of cytokines in the lower genital tract early in pregnancy compared with white women resulting in their increased rate of preterm delivery. These racial differences are explained by the effect of both environmental factors and cytokine promoter genetic polymorphisms. Evaluating the pre-pregnant cytokines, endometrial histology, and cytokine promoter phenotype will help us determine whether pre-pregnant upper genital tract infection raises lower genital tract cytokines and increases the risk of preterm delivery. Specific Aims: To assess the relationship of concentration of pro-inflammatory cytokines (IL-1Beta, IL-6, IL-8, and TNF-alpha) and anti-inflammatory/regulatory cytokines (IL-4, IL-10, IL-1 receptor antagonist, TNF-alpha soluble receptor, and TGFBeta1) in the lower genital tract early in pregnancy with subsequent preterm birth; To evaluate the effect of

race on concentration of pro- and anti-inflammatory products in the lower genital tract early in pregnancy; To assess, by race, the impact of environmental factors and cytokine promoter genetic polymorphisms on the concentration of pro- and anti-inflammatory products in the lower genital tract; To evaluate the relationship of pre-pregnancy histologic **endometritis** with proinflammatory cytokine promoter phenotype, genital cytokine levels before and during pregnancy, and preterm delivery. Methods: To fully investigate the intricate relationship between cytokine concentrations and adverse pregnancy outcome we will perform an observational, prospective, longitudinal study of 400 white and 400 African-American women seeking prenatal care from Magee-Women's Hospital antepartum clinics. Blood and cervical specimens will be obtained for the measurement of cytokine promoter gene polymorphisms, genital cytokine production, and genital bacteria at 16 and 26 weeks gestational age. Interview and biologic measures will be used to assess epidemiologic risk factors for preterm birth. An additional small cohort (n=200) of women will be enrolled to show the relationship between pre-pregnant upper genital tract **endometritis,** bacterial infection, genital cytokines measured early in pregnancy, proinflammatory cytokine promoter phentoype, and the risk of preterm birth.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: STDS AND THE PATHOGENESIS OF SUBCLINICAL PID**

  Principal Investigator & Institution: Sweet, Richard L.; Professor and Chair; Magee-Women's Hospital of Upmc 300 Halket St Pittsburgh, Pa 15213

  Timing: Fiscal Year 2001; Project Start 01-MAY-1998; Project End 30-APR-2003

  Summary: Unrecognized pelvic inflammatory disease (PID) may be a major factor in the pathogenesis of tubal factor infertility. This is supported by the presence of serologic evidence of prior sexually transmitted diseases (STD's) in a large proportion of women with tubal factor infertility, yet most of these women do not recall a history of STD's or PID. In addition, many women with lower genital tract infection associated with STD's (gonorrhea, chlamydia, bacterial vaginosis) have histologic evidence of **endometritis** even though they do not have symptoms of PID. Our hypothesis is that unrecognized PID due to STD's is associated with tubal obstruction. We propose to test this hypothesis in a cohort of 1500 women aged 15-30 with lower genital tract STD associated infection. A group of 200 women with acute symptomatic PID will be evaluated for comparison. Specimens will be obtained from the vagina and cervix for microbiologic analysis and measurement of defensins (neutrophil granule products). An endometrial biopsy will be obtained for histologic and microbiologic analysis. The primary outcome of this study is tubal impatency, therefore all women will undergo a hysterosalpingogram 12 weeks from enrollment. Other outcomes include infertility and ectopic pregnancy formation, which will be determined using regular telephone contact for at least one year to determine the rate of adverse reproductive sequelae. The frequency of tubal impatency will be compared between women with acute symptomatic PID, women with unrecognized PID, and uninfected women. The risk of unrecognized PID will be compared between women testing positive for an STD and uninfected women. As the diagnostic accuracy for the diagnosis of PID is currently suboptimal, risk factors for unrecognized PID will be established, a clinical prediction model will be devised, and defensins from the lower genital tract will be evaluated as less-invasive markers of PID. The microbiology and histology of unrecognized PID will be compared to these findings in acute PID, in an effort to understand the pathogenesis of PID. Information obtained from this study will: i) determine the role of unrecognized PID in subsequent tubal damage ii) establish risk factors and predictors of PID iii)improve the understanding of

the pathogenesis of PID. Earlier detection of unrecognized PID will enable more timely treatment, with the intent on reducing the rate of tubal impatency and resultant adverse reproductive sequelae.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: THE ACQUISITION OF BACTERIAL VAGINOSIS IN LESBIANS**

  Principal Investigator & Institution: Marrazzo, Jeanne M.; Medicine; University of Washington Seattle, Wa 98195

  Timing: Fiscal Year 2002; Project Start 15-SEP-2002; Project End 31-AUG-2007

  Summary: (provided by applicant): Bacterial vaginosis (BV) results from a shift in the microbial ecosystem of the vagina from Lactobacillus predominance to overgrowth by anaerobic and facultative species, and has been associated with postpartum/postabortal **endometritis,** preterm birth, pelvic inflammatory disease, and human immunodeficiency virus acquisition. The etiology of BV is unclear, as is the role of sexual transmission of an undefined precipitant. BV frequently recurs in women who initially respond to standard antibiotic therapy. More effective interventions to prevent and treat BV require an understanding of the role of sexual transmission. Relative to most heterosexual women, lesbians have a two to three-fold higher BV prevalence (25 percent-52 percent). Preliminary evidence strongly implicates sexual transmission of vaginal secretions between women as a risk for BV. The proposed work will define the temporal association between sexual practices that transfer vaginal secretions and BV acquisition, and design an intervention to prevent this transfer and test its efficacy in reducing BV recurrence. Specific aims are: (1) prospectively define risk factors associated with acquisition of BV in a cohort of lesbians, including sexual practices that transfer vaginal secretions, sex with men, lubricant use, douching, menses, and changes in vaginal lactobacilli. The hypothesis is that BV in lesbians occurs after sexual transmission of vaginal fluid from a woman with BV to a woman without BV; that women not colonized with vaginal hydrogen peroxide-producing lactobacilli will be at highest risk for BV acquisition by this mechanism; and that comparative analyses of vaginal flora in sex partners will show similar microbial profiles. (2) Test the efficacy of an intervention to reduce transfer of vaginal fluid between female sex partners in reducing recurrence of BV following treatment with metronidazole in a prospective, randomized trial. The hypothesis is that the intervention will improve knowledge, attitudes, beliefs, and intention about BV prevention, reduce sexual exposures that increase risk of transfer of vaginal fluid, and reduce rates of BV recurrence. Lesbian couples provide a unique opportunity to conduct comparative studies of vaginal microbial ecology in sex partners, and to directly analyze determinants of transmission.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

The National Library of Medicine: PubMed

One of the quickest and most comprehensive ways to find academic studies in both English and other languages is to use PubMed, maintained by the National Library of Medicine.[3] The advantage of PubMed over previously mentioned sources is that it covers a greater

[3] PubMed was developed by the National Center for Biotechnology Information (NCBI) at the National Library of Medicine (NLM) at the National Institutes of Health (NIH). The PubMed database was developed in conjunction with publishers of biomedical literature as a search tool for accessing literature citations and linking to full-text journal articles at Web sites of participating publishers. Publishers that participate in PubMed supply NLM with their citations electronically prior to or at the time of publication.

number of domestic and foreign references. It is also free to use. If the publisher has a Web site that offers full text of its journals, PubMed will provide links to that site, as well as to sites offering other related data. User registration, a subscription fee, or some other type of fee may be required to access the full text of articles in some journals.

To generate your own bibliography of studies dealing with endometritis, simply go to the PubMed Web site at **http://www.ncbi.nlm.nih.gov/pubmed**. Type "endometritis" (or synonyms) into the search box, and click "Go." The following is the type of output you can expect from PubMed for endometritis (hyperlinks lead to article summaries):

- **A case of primary amenorrhea caused by tuberculous endometritis.**
  Author(s): Anuman-rajadhon Y.
  Source: J Med Assoc Thai. 1970 February; 53(2): 142-7. No Abstract Available.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=5476908&dopt=Abstract

- **A case-control study on post-caesarean endometritis-myometritis in Mozambique.**
  Author(s): Libombo A, Folgosa E, Bergstrom S.
  Source: Gynecologic and Obstetric Investigation. 1995; 39(3): 180-5.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=7789913&dopt=Abstract

- **A clinical and microbiologic analysis of risk factors for puerperal endometritis.**
  Author(s): Newton ER, Prihoda TJ, Gibbs RS.
  Source: Obstetrics and Gynecology. 1990 March; 75(3 Pt 1): 402-6.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=2406660&dopt=Abstract

- **A clinical double-blind study on the effect of prophylactically administered single dose tinidazole on the occurrence of endometritis after first trimester legal abortion.**
  Author(s): Westrom L, Svensson L, Wolner-Hanssen P, Mardh PA.
  Source: Scand J Infect Dis Suppl. 1981; 26: 104-9.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=6941445&dopt=Abstract

- **A clinicopathological study of IUD users with special reference to endometrial patterns and endometritis.**
  Author(s): van Bogaert LJ.
  Source: Gynecologic and Obstetric Investigation. 1983; 16(3): 129-35.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=6618283&dopt=Abstract

- **A comparison of once-daily and 8-hour gentamicin dosing in the treatment of postpartum endometritis.**
  Author(s): Del Priore G, Jackson-Stone M, Shim EK, Garfinkel J, Eichmann MA, Frederiksen MC.
  Source: Obstetrics and Gynecology. 1996 June; 87(6): 994-1000.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=8649712&dopt=Abstract