Abstracts From

the

Third Annual Meeting of the
International Infectious Disease
Society for Obstetrics and
Gynecology USA

New Orleans, Louisiana
May 9–10, 1998
International Infectious Disease Society for Obstetrics and Gynecology USA

MEMBERSHIP ROSTER

H. Hugh Allen, MD
Joseph Apuzzio, MD
Kevin Ault, MD
David A. Baker, MD
Jorge D. Blanco, MD
Doris Brooker, MD
Michael S. Burnhill, MD
Sebastian Faro, MD, PhD
Larry C. Ford, MD
Stephen Fortunato, MD
Larry C. Gilstrap III, MD
Douglas Glover, MD
Jennifer Gunter, MD
Hunter A. Hammill, MD
David L. Hemsell, MD
Hans A. Hirsch, MD
Mahmoud A. Ismail, MD
Jan Jeremias
A. Karen Kreutner, MD
Bryan Larsen, PhD
John W. Larsen Jr, MD
William J. Ledger, MD
Charles H. Livengood III, MD
Maurizo Maccato, MD
James MacGregor, MD, CM
Mark Martens, MD
Barbara L. McFarlin, RN
S. Gene McNeeley Jr., MD
Lane Mercer, MD
Gilles R.G. Monif, MD
Susan Marie Mou, MD
Paul Nyirjesy, MD
Newton G. Osborne, MD
Joseph G. Pastorek II, MD
Mark Pearlman, MD
Phillip Pinell, MD
David E. Soper, MD
Paul Summers, MD
Lin Tao, MD
Jessica L. Thomason, MD
Miklos Toth, MD
Ernst R. Weissenbacher, MD
Steven Witkin, PhD
DETECTION OF CHLAMYDIAL ANTIGENIC MATERIAL IN OVARIAN, PROSTATIC, ECTOPIC PREGNANCY AND SEMEN SAMPLES OF CULTURE NEGATIVE SUBJECTS.
Toth M, Patton D, Campbell LA, Sewchuk M, Ledger W and Chervenak F. Department of Obstetrics and Gynecology, Cornell University Medical College, New York, New York; Department of Obstetrics and Gynecology and Pathobiology, University of Washington, Seattle, Washington; Department of Pathology, Lenox Hill Hospital, New York, New York.

Objective: The pathogenesis of long-term sequelae in Chlamydia trachomatis infection, is poorly understood. While serology indicates previous chlamydial infection, cultures or even polymerase chain-reaction (PCR) studies are frequently negative. It is not known whether the bacterium is absent or persists in a dormant state where it evade detection.

Methods: Using immunoperoxidase (IP) staining and in situ hybridization (ISH), we examined tissues of PCR and culture negative subjects. Ovarian biopsy specimens from 19 PCR negative women with pelvic adhesions and/or tubal infertility were analyzed by both methods. Samples of prostates from 10 culture negative men undergoing prostatectomy for benign hypertrophy, semen samples from PCR negative sexual partners of 14 women with PID and/or ectopic pregnancy were examined by PCR only.

Results: Seven of the 19 ovarian specimens tested positive for chlamydia antigen or DNA (36%). Of the 10 hypertrophic prostates examined, four (40%) was positive. Of the 14 semen samples examined, three (21%) tested positive. Tissue samples of three cases of ectopic pregnancy (EP) were positive by IP. Five of the seven patients with positive ovarian findings were seropositive. All IP positive ectopic pregnancy and semen patients were also seropositive for C. trachomatis.

Conclusions: 1. Chlamydia trachomatis antigen and nucleic acid can be frequently demonstrated in asymptomatic, PCR or culture negative men and women with chronic infection. 2. Chlamydia antigens may have an etiologic role in benign prostatic hypertrophy and ectopic pregnancy. 3. Antigenic material may be sexually transmissible. 4. IP and ISH identify temporarily inactive bacteria that may continue to act as immunostimulants and potentially reactivate as chlamydia infection.

ANTIBODIES TO THE OMP2 ANTIGEN OF CHLAMYDIA TRACHOMATIS IN WOMEN WITH TUBAL FACTOR INFERTILITY. Ault K, Ruther P, Webb A and Basick N. University of Iowa Hospitals and Clinics, Iowa City, Iowa.

Objective: To determine the prevalence of antibodies to the Chlamydia trachomatis antigen, omp2.

Methods: Subjects for this study were women with tubal factor infertility. Tubal factor infertility was defined as one year of regular unprotected intercourse without conception with hydrosalpinx or distal tubal occlusion at hysterosalpingogram or laparoscopy. Women were excluded from this group if any other cause of infertility was found. Controls were women with patent fallopian tubes and infertility due to their male partner. Antibodies were measured by a prototype enzyme linked immunosorbent assay (ELISA) with omp2 as the antigen (GenBio, San Diego, California). Additionally, women were also tested for antibodies against elementary bodies of Chlamydia trachomatis serovar L2. Cut-off values for the omp2 ELISA were determined by testing the sera of 31 pregnant women that tested negative for antibodies against Chlamydia trachomatis elementary bodies. The cut-off was determined by the mean absorbance plus three standard deviations of the sera samples from the pregnant group.

Results: Seventeen of 34 subjects had antibodies to omp2 by our prototype ELISA. Two of 48 controls had antibodies to this antigen (p<0.005 by chi square).

Conclusions: Antibodies to omp2 can be correlated to tubal factor infertility, a common gynecological problem known to be caused by prior infection with Chlamydia trachomatis.

COMPARISON OF PACE, AMPLIFIED CHLAMYDIA TRACHOMATIS (CT) ASSAYS—TRANSCRIPTION MEDIATED AMPLIFICATION (AMP CT) AND LIGASE CHAIN REACTION (LCX), AND CLEARVIEW EIA FOR CT. Landers L, Lauderdale TL, Thorenscroft I and Chapin K. University of South Alabama (USA), Mobile, Alabama.

Screening of STDs in a greater proportion of sexually active patients has become an accepted protocol by most healthcare providers. The purpose of this study was to compare the current test methods for CT used at USA: PACE CT (Gen-Probe) and Clearview CT EIA (Wampole Laboratories) with the amplified technologies Amp CT (Gen-Probe) and LCx CT (Abbott). In addition, a number of demographic parameters were ascertained by questions asked at the time of examination. One urine and four endocervical swabs obtained in random order were collected from 786 female patients attending 1 of 4 OB/GYN clinics (87% of patients had no STD-related symptoms). Patients were considered positive for CT if three or more assays (swab and/or urine) were positive. Abbott and Gen-Probe confirmed discrepant results by alternate amplified assays. There were a total of 66 true positives detected by the combination of endocervical swabs and urine specimens. After discrepant analysis, sensitivities for endocervical swab specimens for EIA, PACE, LCx, and Amp CT were 71, 85, 95, and 100% respectively. Sensitivities for Amp CT and LCx urine specimens were 86 and 97%, respectively. Prevalence of CT was 8.2% as determined by amplified technology, yet only 5.6% with the current method most commonly used in the clinics (Clearview). Overall, the amplified technologies were the most sensitive method using either swab (Amp CT) or urine (LCx). PACE offered the advantage of a simpler and less expensive assay with acceptable sensitivity. Clearview CT EIA, while yielding a rapid in-office result, has unacceptably low sensitivity. Advantages, disadvantages and considerations for implementation of STD test methods will be presented.

A RANDOMIZED, CONTROLLED MOLECULAR STUDY OF CONDYLOMATA ACUMINATA CLEARANCE DURING TREATMENT WITH IMIQUIMOD. Tomain MA, Miller RL, Arany I, Tyring SK, McDermott DJ, Parrish SL, Smith MH, and Slade HB. 3M Pharmaceuticals, St. Paul, Minnesota; University of Texas Medical Branch, Galveston, Texas.

Imiquimod cream 5% has recently become available in the United States for the treatment of external genital and perianal warts caused by human papillomavirus (HPV). One objective of these studies was to determine cytokine induction following topical Imiquimod application to hairless mice and in a Phase I vehicle controlled study, to human genital wart patients. A second objective of the human study was to measure effects of drug treatment on cell
patients. In the mouse study, biopsies were taken at the treatment site and from the other side of the mouse at the time of drug application at 1 hour and at 2 hours. In humans, biopsies of the wart treatment site were taken at drug initiation, at six weeks and at the end of 16 weeks treatment or wart clearance. Human biopsies were taken at the end of 16 weeks treatment or wart clearance. IFN-α protein were significantly decreased, and wart size was decreased in all patients treated with Imiquimod in this study. These results indicate that topical Imiquimod is an effective local cytokine inducer in skin and an effective treatment for HPV lesions in humans.

GROUP A STREPTOCOCCUS IN THE GYNECOLOGIC PATIENT. Garvey P and Ledger WJ. The New York Hospital—Cornell Medical Center, New York, New York.

Background: Serious Group A Streptococcal (GAS) infections have a complex pathophysiology. Newly discovered streptococcal pyogenic exotoxins A, B and C appear to induce significant T cell proliferation and initiate the production of large quantities of tumor necrosis factor, interleukins and various cytokines through a unique antigen-processing mechanism, leading to drastic and widespread tissue damage and shock. In addition, GAS infections involving the female reproductive tract may not be associated with foreign bodies or recent endometrial disruption as was previously thought.

Case: After reviewing the medical records of all inpatients with GAS blood cultures at New York Hospital between the years of 1996 to present, a total of four female patients were identified who presented with an acute abdomen and septicemia. In each case, their symptoms were severe and developed rapidly. The differential diagnosis upon presentation was severe pelvic inflammatory disease versus perforated viscus. All four were in their early 40’s and none had any recent tampon use. One patient was three weeks postpartum. The other three had no recent endometrial instrumentation or trauma. Three out of the four underwent emergent abdominal exploration which revealed only peritonitis. All improved dramatically after aggressive irrigation of the pus in their abdominal cavities and administration of antibiotics. The patient who did not undergo exploration or irrigation died several days after presentation.

Conclusion: Although the seriousness of GAS infections may be secondary to toxin-mediated pathophysiology, reducing the production of the toxin by eliminating the organism is key to the management. Appropriate and aggressive use of antibiotics and reducing bacterial load through debridement and irrigation are crucial in treating serious GAS infections. In addition our investigation seems to indicate that the risk factors for serious GAS in the gynecologic patient may be changing. The aggressive use of antibiotics in treating mild GAS infections during childhood may have altered the epidemiology of GAS infection in adults.

ABSTRACTS

HEPATITIS B AND PREGNANCY—A CHALLENGE FOR OBSTETRICS IN DEVELOPING COUNTRIES. Duarte G, Mussi-Finhata MM, Martinez R, Landers DV, Neuer A and Giraldo P. University of Sac Paulo, SP (Brazil); University of Pittsburgh, Pittsburgh, Pennsylvania, Cornell University Medical College, New York, New York.

Immunoprophylaxis of neonates from mothers who are seropositive hepatitis B surface antigen (HBsAg) is a challenging task in developing countries. This study comprised 7992 healthy women who delivered in the Hospital of Ribeirao Preto Medical School, University of Sac Paulo (Brazil), in order to determine the rates of HBsAg prevalence, other markers of hepatitis B virus and to establish a correct, cheap and sustainable way to identify these women. Two steps of ELISA procedure were performed in the serum samples. A general 2-hour incubation screening test for HBsAg was used first. Those samples that were positive in the screening test underwent an 18-hour confirmation testing. The samples confirmed positive were submitted to anti-HBsAg, anti-HBeAg, anti-HBcAg and anti-HBcAg testing. The screening tests found 84 of the 7992 samples (1.05%, 95% CI: 0.84-1.30) to be positive for HBsAg; however, only 76 were confirmed positive (0.95%, 95%
ABSTRACTS

CI: 0.75-1.19). The rate of HBsAg positive was significantly higher in patients whose pregnancies ended in miscarriage (1.84%) compared to term controls (84%, p<0.005). Risk factors for HBV infection by amniocentesis alone detected only 27.6% of the confirmed HBsAg positive subjects. HBeAg was found in 21.3% of all positive patients, indicating a high risk of vertical transmission of the virus in this population. These results demonstrate a need to conduct specific serology research at term in order to provide effective neonatal immunoprophylaxis. Screening for HBV infections is a cheaper alternative in developing countries than the universal immunoprophylaxis among newborns.

INITIAL EVIDENCE FOR PHAGE INFECTION AND TRANSMISSION IN VAGINAL LACTOBACILLI. Tao L, Pavlova S, Alpay S, and Kilic A. University of Missouri, Kansas City, Missouri; Karadeniz Technical University, Trabzon, Turkey.

Objective: Bacterial vaginosis (BV) is associated with an unplanned decrease of vaginal lactobacilli. We have previously identified phages in vaginal lactobacilli, suggesting that phage infection may occur in women. The aims of this study are to determine whether phages can infect lactobacilli in vivo in women and be transmitted among different women.

Study Design: Among 60 vaginal lactobacillus lysogenic strains isolated from 207 American and Turkish women, five strains in two groups were selected for this study because the phages of each group of strain showed a similar host range. The first group included two lactobacillus strains from an American woman, and the second group included three strains from three unrelated Turkish women residing in different geographic areas. The temperate phages of these strains were analyzed by electron microscopy, host range and DNA fingerprinting, whereas the lactobacillus host strains were analyzed by protein profiles and AP-PCR.

Results: The two lactobacillus strains, KC012a and KC012b, from the American woman showed different protein profiles by SDS-PAGE, but their phages had identical DNA fingerprints, indicating that the two bacteria were infected by the same phage. On the other hand, the three lactobacillus, TL034c, TL074c and TL076c, from three different Turkish women were found to release an identical phage by DNA fingerprinting. However, the protein profiles and AP-PCR patterns of the two Turkish strains, TL034c and TL074c, were identical, but the third one was different.

Conclusion: These results provided initial evidence that phage infection may occur in vaginal lactobacilli in vivo in women and that lactobacillus phages may be transmitted among different women either as a prophage in its host bacterium or as a free phage by itself.

TEMPERATURE CHANGES AT PARTURITION. Bartholomew ML, Ashkin E, Schifflman A and Larsen J. Department of Obstetrics and Gynecology, The George Washington University Medical Center, Washington, DC.

Objective: To evaluate the normal trend in maternal temperature variation during labor and the early postpartum period.

Study Design: A retrospective chart review of 123 consecutive singleton deliveries during 1996 was conducted. All available sublingual temperatures were collected from the time of admission to the L&D area. Study subjects were defined as being 36 weeks gestation without medical problems associated with infectious morbidity. Three mutually exclusive clinical groups of patients were defined: (1) no clinical chorioamnionitis and no antibiotics given in labor, (2) no clinical chorioamnionitis but prophylactic antibiotics given in labor, and (3) presence of clinical chorioamnionitis. The temperatures (Celsius) were divided into two temporal groups: those taken during labor, and those taken during recovery. For each group, the maximum temperatures (Tmax) of each patient were averaged, and standard deviations were calculated. Inter and intra-group comparisons of the average Tmax were performed using Student T-tests. Inter-group comparisons were made only between Group 1 and 2 due to small sample size of Group 3.

Results: Of the 123 patients, 101 (82.1%) met the inclusion criteria for normal term parturients; 74.3% (N = 75) of all normal parturients had Tmax at or below 37.5, and only 5.9% (N = 7) had temperatures 38.0. The average Tmax in labor for Groups 1, 2, and 3 were 37.0 ± 0.42 (N = 57), 36.9 ± 0.5 (N = 29), and 38.0 ± 0.3 (N = 5), respectively. The average Tmax in recovery for Groups 1, 2 and 3 were 37.1 ± 0.49 (N = 56), 37.0 ± 0.58 (N = 28) and 37.9 ± 0.1 (N = 4). There were no significant differences between the labor and recovery Tmax within groups. There were no significant difference in Tmax between Groups 1 and 2; therefore, a weighted mean Tmax of 37.0 ± 0.45 was calculated.

Conclusion: In normal term parturients without clinical chorioamnionitis, labor does not appreciably increase maternal temperature above normal body temperature; 85.7% of patients in labor had a Tmax less than 37.5. If 2 standard deviations are used to define the maximum temperature boundaries in these patients, then the range would be between 36.1-37.9. Fever in labor has been defined as a temperature 38.0. Further studies are needed to correlate temperatures > 37.5 with maternal and neonatal infectious morbidity in order to more clearly define fever in labor.

RELEVANCE OF POLYMORPHISMS IN IMMUNE REGULATORY GENES IN WOMEN UNDERGOING IN VITRO FERTILIZATION. Jeremias J and Witkin SS. Cornell University Medical College, New York, New York.

Differences in the individual host’s immune response, not only microbial virulence factors, are important in determining the sequela to infection. We examined by polymerase chain reaction polymorphisms in women undergoing IVF in three genes involved in immune regulation: the tumor necrosis factor-α (TNF-α) promoter, interleukin-1 receptor antagonist (IL-1ra) and the inducible 70kD heat shock protein (hsp70). In couples whose infertility was due to a male factor, 73.3% of the women were heterozygous for the 1, 2 alleles of the IL-1ra gene. This prevalence was higher (p = 0.01) than that present in women with tubal infertility (20.0%). In contrast, there was no significant difference in TNF-α promoter alleles and infertility due to the male or female factors. A specific TNF-α promoter allele, but not ab IL-1ra allele, was associated with increased induced ovalation. Women heterozygous for the two predominant TNF-α promoter alleles had a mean of 18.0 oocytes harvested as opposed to 11.1 oocytes from women homozygous for the most prominent allele (0.009). Lastly, women with bacterial vaginosis had a higher prevalence for the homozygous B, B allele of the hsp70 gene (4/8, 50%) than did unselected IVF patients (25/191, 13%). Continued analysis of these and other immune-related genes in women with defined infectious and non-infectious sequela will further clarify the role of host genetic factors in susceptibility to specific outcomes.

RELATION BETWEEN SEXUAL ACTIVITY, IMMUNITY TO 60 KD HEAT SHOCK PROTEINS (hsp60) AND TUMOR NECROSIS FACTOR (TNF) IN FEMALE ADOLESCENTS FROM IVANOVO, RUSSIA. Xoneeva I, Neuer A, Somiokeza N, Posiiseyeva I, Witkin SS, Ivanovo Research Institute of Maternity
The effects of coitus on immunity to hsp60 and induction of a pro-inflammatory cytokine were examined in 45 teenage girls age 13–17; 63% of the girls were sexually active while 37% were virgins. Gential tract infections were present in 53% of the girls which was highly correlated with non-virgin status (p=0.006). Sera were tested by ELISA for IgG antibodies to bacterial (Escherichia coli GroEL) and human hsp60 using the purified recombinant proteins as standards. Circulating TNF concentrations were determined by commercial ELISA. Anti-bacterial and anti-human hsp60 were detected in 10 (22.2%) and eight (17.8%) of the subjects respectively. Thirteen (28.9%) teenagers were positive for pro-inflammatory cytokine were examined in 45 teenage girls age 13–17; 63% of the girls were sexually active while 37% were virgins. Gential tract infections were present in 53% of the girls which was highly correlated with non-virgin status (p=0.006). Sera were tested by ELISA for IgG antibodies to bacterial (Escherichia coli GroEL) and human hsp60 using the purified recombinant proteins as standards. Circulating TNF concentrations were determined by commercial ELISA. Anti-bacterial and anti-human hsp60 were detected in 10 (22.2%) and eight (17.8%) of the subjects respectively. Thirteen (28.9%) teenagers were positive for pro-inflammatory cytokine.

Contrast, there was no relationship between autoantibodies reactive with human hsp60 and virgin (18.8%) or non-virgin (17.2%) status. Detection of TNF correlated with the presence of antibodies to either bacterial hsp60 (p=0.02) or human hsp60 (p=0.03). However, there was no relationship between antibodies to bacterial hsp60 and antibodies to human hsp60. We conclude that sexual intercourse can sensitize teenage girls to bacteria-specific epitopes of hsp60 and that this is associated with induction of a pro-inflammatory cytokine. Autoimmunity to one's own hsp60, which is also associated with TNF activation, can also be detected in some teenagers but is unrelated to coitus or immunity to bacterial hsp60.

INTERVAL BETWEEN CERVICAL CONIZATION AND VAGINAL OR ABDOMINAL HYSTERECTOMY WITH PROPHYLAXIS AND IMPACT ON THE INCIDENCE OF POSTOPERATIVE PELVIC INFECTION RISK. Hemsell DL, Johnson ER, Hemsell P and Nobles B, University of Texas, Southwestern Medical Center at Dallas, Parkland Health and Hospital System, Dallas, Texas.

Most data relating to the interval between cervical conization and hysterectomy and increased postoperative pelvic infection risk were collected prior to routine antibiotic prophylaxis at hysterectomy. General recommendations have been that if hysterectomy could not be performed within three days, the gynecologic surgeon should wait six weeks to decrease postoperative infection risks. No comparative data for vaginal and abdominal hysterectomy for benign disease can be found. Of 539 women enrolled in prospective hysterectomy prophylaxis studies who underwent conization prior to hysterectomy in Parkland Hospital between 1978 and 1995, 48 (8.9%) developed major pelvic infection. Of 422 women undergoing vaginal hysterectomy, 28 (6.6%) developed infection compared with 20/117 (17.1%) women undergoing abdominal hysterectomy (p=0.001). After vaginal hysterectomy, any interval from 0 (frozen cone) to 120 days did not affect the postoperative infection rate (p=0.59). The interprocedure interval after abdominal hysterectomy was important; 20/90 (22.2%) women with an interval from 0-7 days became infected postoperatively compared with 0/27 women whose interprocedure interval was 8-120 days (p=0.003). Infection rate was highest when the interval was 4-7 days. Most (81%) infections developed before discharge from the hospital; however, 33% of infections after vaginal hysterectomy were late. Of all late infections (nine), four (44%) were pelvic abscesses, two (22%) were infected pelvic hematomas, and one (11%) was an abdominal incision infection. Infection type and incidence were related to the prophylactic regimen administered at hysterectomy. Current surgery scheduling and prophylaxis are based on these data.

WOUND INFECTION AFTER CESAREAN SECTION: EFFECT OF SUBCUTANEOUS TISSUE DEPTH. Soper DE* and Lamotte C. Department of Obstetrics and Gynecology, Medical University of South Carolina, Charleston, South Carolina.

Objective: To determine the effects of subcutaneous tissue depth on the wound infection rate after cesarean section (CS).

Study Design: Women undergoing CS were prospectively observed for the occurrence of wound infection at six weeks postpartum. Demographic and clinical variables were assessed as possible risk factors for wound infection. Surgical technique and prophylactic antibiotic administration were standardized. Maximum vertical depth of the subcutaneous tissue was measured prior to skin closure. Risk factors for wound infection were assessed by univariate analyses. Subsequently, all significant variables were included in a multiple regression analysis.

Results: Wound infection occurred in 10 of 75 (13.3%) women undergoing CS. Risk factors significantly associated with wound infection by univariate analysis included depth of subcutaneous tissue (p=0.01), maternal weight (p=0.01), body surface area (p=0.001), and postoperative hemoglobin (p=0.0004). Subcutaneous tissue depth was the most significant risk factor for wound infection (p=0.014) following multiple regression analysis. Seventy percent of wound infections occurred in women with a depth of 4 cm.

Conclusion: The incidence of wound infection following cesarean section in our patient population is 13.3%. Subcutaneous tissue depth is the most significant risk factor for wound infections following CS.

INFLAMMATORY STREPTOCOCCAL VAGINITIS. Gunter J, Ranallo L, Tawfik O, University of Kansas Medical Center, Kansas City, KS.

Objective: Streptococcus agalactiae has infrequently been reported as a cause of vulvovaginitis. This report describes a cohort of women with inflammatory vaginitis secondary to vaginal infection with S. agalactiae.

Methods: A prospective study of women with vulvovaginitis referred to a university vaginitis clinic identified six women with inflammatory vaginitis and positive vaginal cultures for S. agalactiae. All patients were evaluated by history and physical, vaginal pH, wet mount, amine tests and vaginal cultures. Inflammatory vaginitis was defined as an increased ratio of polymorphonuclear leukocytes to epithelial cells in a least four high-power fields. No patient had evidence of upper genital tract infection, cervicitis or trichomonas.

Results: All six patients complained of vulvovaginal burning or pruritis and also of dyspareunia, 83% (5/6) complained of excessive vaginal discharge, and one patient complained of a vaginal odor. On examination all patients had vulvar and vaginal erythema and an adherent vaginal discharge, 2/6 patients had vulvar lesions and one had an intense hemorrhagic vaginitis. The pH ranged from 4.5-6.0 and all patients had a negative amine test. Wet mount revealed an inflammatory vaginitis and cultures were positive for S. agalactiae. Patients were treated with a 2-week course of oral antibiotics (pencillin V or sulfamethoxazole/trimethoprim) and topical estrogen cream. After one course of treatment, 4/6 patients were symptom free and the remaining two had a 75% improvement in symptoms.
ABSTRACTS

These patients had a complete resolution of symptoms with a second course of treatment.

Conclusion: Streptococcal vaginitis must be considered in a patient with an inflammatory vaginitis refractory to other treatments. The hallmark of this disease is vulvar and vaginal erythema accompanied by a purulent discharge and an intense burning or pruritus. Our cohort was responsive to an oral anti-streptococcal agent combined with topical estrogen cream suggesting that a local estrogen deficiency may have some role in the etiology of this disease.

THE IN VITRO AND IN VIVO EFFECTS OF INNER CONFIDENCE VAGINAL SUPPOSITORIES ON POSTCOITAL pH. Ford LC*, Kesler VP, Ford LC Jr, Ford SD, Hammill HA and Lebherz TB. Department of Obstetrics and Gynecology, University of California-Irving Medical Center, Orange, California; LaFor Laboratories, Newport Beach, California; Department of Obstetrics and Gynecology, Baylor, Houston, Texas; Department of Obstetrics and Gynecology, University of California-Los Angeles, Los Angeles, California.

It has been known since the 1960’s that the intravaginal pH increases postcoitally. These reported pH elevations can persist as long as eight hours after a single act of intercourse. The elevated vaginal pH can promote Candida as well as other types of infections in predisposed individuals. It was found that all of the commercially available spermicidal products studied, elevate the pH, both in vitro and in vivo to above pH 6.5, even in the absence of the basic proteins found in semen. We found that the organic acid buffer systems found in Inner Confidence vaginal suppositories lowered semen samples in vitro from above pH 8 to pH 4.5. The presence of the Inner Confidence vaginal suppositories were also found to prevent the postcoital rise in intravaginal pH, maintaining a pH of 4.5 for over eight hours. In monogamous couples, Inner Confidence vaginal suppositories were found to both increase the cervical mucous viscosity and destroy any sperm or white cells present as compared to “normal PCT’s” during the cycles prior to the use of Inner Confidence vaginal suppositories. These studies are in agreement with the WHO and NIH mandates that the ideal vaginal microbicidal should maintain an acidic vaginal pH throughout all the phases of sexual activities. The implications of these observations will be discussed.

IMMUNITY TO THE 10kD CHLAMYDIAL HEAT SHOCK PROTEIN, CHLAMYDIAL LPS AND THE 60 kD E. COLI HEAT SHOCK PROTEIN (GroEL) IN PATIENTS WITH PRETERM LABOR. Neuer A, Korneeva I, Dieterle S, Giraldo P, Herdecke, Germany; Department of Med. Microbiology, University of Witten/Herdecke, Germany; Department of Med. Microbiology, University of Wisconsin, Madison, Wisconsin.

The etiology of preterm labor is multifactorial and not very well understood. Microbial infections are well established risk factors contributing to preterm labor. Microbial heat shock proteins (hsp) represent major microbial antigens and early targets of the bacterial immune response. The expression of a 10kD chlamydial hsp (chsp10) has been shown to be indicative of a persistent chlamydial upper genital tract infection. The aim of this study was to define the relation between preterm labor and circulating antibodies to chsp10 and other common microbial antigens like GroEL and chlamydial LPS. The study group consisted of 41 hospitalized patients with preterm labor treated with i.v. tocolytics and 50 asymptomatic term controls. Lower genital tract infections were ruled out by culture and PCR. IgG antibodies to chsp10, GroEL, chlamydial LPS as well as levels of interleukin-6 (IL-6) in sera were determined by ELISA. Chsp10 antibodies were more prevalent in patients with preterm labor (24% vs. 12%, p<0.02). In addition, chsp10 was associated with the expression of the pro-inflammatory cytokine IL-6. In contrast IgG to GroEL (34% vs. 14.6%, p=0.05) and chlamydial LPS (0% vs. 26.8%, p=0.001) were more prevalent in patients with term labor and were not associated with IL-6. The humoral immune response to chlamydial hsp10 is associated with both interleukin-6 induction and preterm labor, thus indicating probably an ongoing upper genital tract infection in these patients. Immunity to chlamydial LPS and GroEL, more likely reflects a previous exposure to these organisms without negative impact on preterm labor.


Objective: This study was conducted to assess whether there was any association between bacterial vaginosis and pregnancy complications in real-life, uncontrolled clinical settings.

Design: Case-control study where cases included women with pregnancy complications (including preterm delivery) while controls were women with normal deliveries.

Materials and Methods: The MarketScan® national claims database was used to evaluate eligible women from 1992 to 1994. ICD-9 codes were used to identify normal and preterm deliveries, bacterial vaginosis, and pregnancy complications. The rates of bacterial vaginosis diagnosed during pregnancy were compared between cases and controls. Confounding factors such as age, multiple births, urinary tract infection, previous miscarriage, diabetes, and hypertension were controlled for in the analysis.

Results: A total of 73,548 women in this database had delivery claims during 1992-94. Of these, 59,366 women had normal deliveries. A pregnancy complication or preterm delivery occurred in 14,182 women. Pregnant women with bacterial vaginosis had an increased risk for preterm delivery (OR=1.3, 95% CI=1.0-1.5), pregnancy complications (OR=1.4, 95% CI=1.3-1.6), and preterm delivery accompanied with other pregnancy complications (OR=1.7, 95% CI=1.3-2.0). Results from the multivariate analysis revealed that women with bacterial vaginosis had a 10% increased chance (p=0.002) of preterm delivery (OR=1.1, 95% CI=0.91-1.31), and that bacterial vaginosis was a significant predictor for other pregnancy complications (OR=1.12, 95% CI=1.01-1.25). This association between bacterial vaginosis and pregnancy complications was similar in magnitude to those of other well established risk factors for pregnancy complications and preterm delivery.

Conclusions: A national claims database provides evidence that bacterial vaginosis is a significant risk factor for pregnancy complications. The profound public health concern of these complications may warrant measures such as routine screening for bacterial vaginosis among pregnant women.


INFECTION DISEASES IN OBSTETRICS AND GYNECOLOGY • 147
Objective: To evaluate the effect of extended-release oral metronidazole and clindamycin cream for the treatment of bacterial vaginosis on the health-related quality of life of women.

Materials and Methods: A total of 393 women diagnosed with bacterial vaginosis, who were randomized to treatment with a new, extended-release oral formulation of metronidazole or 2% clindamycin phosphate cream for seven days were included in this analysis. Health-related quality of life, as measured by the SF-12 questionnaire and an evaluation of sexual function, was assessed at baseline (Visit 1), 4–7 days after completion of treatment (Visit 2), and 28–32 days after treatment (Visit 3). At all three visits, the severity of signs and symptoms of bacterial vaginosis (i.e., vaginal odor, vulvovaginal burning, vulvovaginal itching, pelvic pain, vaginal discharge, and discharge consistency) was assessed by patients and physicians. Changes in quality of life and sexual functioning were evaluated.

Results: Evaluation of baseline data revealed that there were no significant differences in patient and physician assessed signs and symptoms of bacterial vaginosis, health-related quality of life, or sexual functioning between the two treatment groups. Baseline mean summary scores for physical health and mental health were significantly lower in women with more severe pelvic pain (p<0.01). In addition, there were significant associations between the severity of vaginal odor, vulvovaginal burning, and vulvovaginal itching, with impaired sexual functioning (p<0.05). Within treatment groups, mental health scores at Visits 2 and 3 significantly improved from baseline (p<0.05). At Visit 3, sexual function scores improved significantly from baseline for both treatment groups (p<0.05). However, at all visits, there were no statistically significant differences in the quality of life and sexual function scores between the treatment groups.

Conclusions: The severity of symptoms associated with bacterial vaginosis may affect the quality of life of a woman in terms of physical health, mental health, and sexual function. This study revealed no differences in quality of life measurements associated with extended-release oral metronidazole or clindamycin cream. The choice of treatment for bacterial vaginosis should be based on the clinical, microbiological efficacies of available treatment regimens.

ESTROGEN MEDIATES CANDIDA ALBICANS ADAPTATION TO ENHANCE IN VIVO SURVIVAL. O’Connor C*, Essmann M, and Larsen B, Drake University and University of Osteopathic Medicine and Health Sciences, Des Moines, Iowa.

Estrogen has been shown in our laboratory to enhance the growth of the pathogenic fungus, Candida albicans. We investigated the physiologic adaptation that potentially enhances the growth and survival of C. albicans by means of studies on tolerance to thermal and oxidative stresses that C. albicans may encounter upon entry into a host. In particular, our preliminary findings with SDS-PAGE shows that estrogen may up-regulate a heat shock protein or protein.

IL-1 AND IL-6 AS MARKERS OF INTRA-AMNIOTIC INFECTION IN PRETERM LABOR. Mandal A, Ratan S, Khandharia R, and Sarin S. Department of Microbiology, GB Pant Hospital and Department of Obstetrics and Gynecology, LNJP Hospital, New Delhi, INDIA.

Thirty cases of preterm labor (PTL>37 weeks of pregnancy) divided into two groups, 15 with intact membranes (IM) and 15 with ruptured membranes (PROM) were monitored for intra-amniotic infections (IAA) by microscopic examination. Aerobic and anaerobic cultures of high vaginal swabs (HVS) and amniotic fluid (AF) were plated on Sabouraud’s Dextrose Agar plates, and colonies were counted. Cultures treated with 17β-estradiol were either shifted from 25°C to 37°C to induce a heat shock response and finally to a lethal temperature of 48.5°C; or control were moved from 25°C to 48.5°C directly. Cultures treated with micromolar or nanomolar 17β-estradiol, were also shifted from 25°C to 48.5°C. After heat treatments, cultures were plated on Sabouraud’s Dextrose Agar plates, and colonies were counted. Cultures which were not treated with 17β-estradiol but were heat adapted (heat shock response induced) exhibited survival percentages as high as 100% of control levels.

We investigated the effects of 17β-estradiol on the susceptibility of cells to oxidative stress using menadione to challenge estrogen treated or untreated Candida albicans. Cultures were grown overnight, supplemented with 17β-estradiol in micromolar or nanomolar concentrations. Cultures were then transferred to media containing 0.001 M menadione. After a one-hour incubation period, surviving yeast were quantified by plate count. Colony counts showed micromolar and nanomolar 17β-estradiol-treated cells were more resistant to menadione treatment than were control cultures. Survival percentages of the 17β-estradiol-treated cultures were as high as 152% compared to controls.

To evaluate changes in cytosolic proteins in response to exposure to estrogen, SDS-PAGE analysis of cell proteins was performed. Cultures were grown to mid-long phase in yeast nitrogen base broth at 25°C without or with 17β-estradiol (micromolar or nanomolar). Yeast cells were lysed vortexing with glass beads (0°C) and particulate debris removed by centrifugation. Proteins were electrophoresed on SDS-PAGE. Protein profiles of several strains exhibited a heat shock-like response. Since 17β-estradiol induced thermotolerance, we compared the cytosolic proteins from estrogen treated yeast with thermally adapted organisms (shifted from 25°C to 39°C for 75 minutes). SDS-PAGE showed that the proteins induced by 17β-estradiol were apparently also induced by heat. We concluded that 17β-estradiol may up-regulate heat shock proteins, which would be consistent with enhanced in vivo survival of C. albicans.

Our findings show that estrogen enhances adaptations to thermal and oxidative stresses that C. albicans may encounter upon entry into a host. In particular, our preliminary findings with SDS-PAGE shows that estrogen may up-regulate a heat shock protein or proteins.
ABSTRACTS

Thus, IL-6 in the amniotic fluid was found to be a better indicator of infection in PTL.


Bacterial vaginosis (BV) is the most frequent cause of vaginal discharge and associated with preterm delivery (PTD). The mechanism of this association is not understood. We investigated the prevalence of BV and its correlation with cervical cytokine production in women undergoing IVF and evaluated its association with outcome. A blinded study of 331 asymptomatic patients undergoing in-vitro fertilization (IVF) was initiated. Patients were evaluated for BV by vaginal gram stain (GS) (Nugent’s criteria), cervical cytokines (IL-1β and IL-8) by ELISA and IVF outcome. BV was determined on the day of retrieval. A cervical swab was collected at this time as well. As standard practice at our institution, all women received tetracycline for four days after retrieval for prophylaxis for possible assisted hatching. 80.7% (267-331) of the women had a normal GS and 19.3% (64/331) had abnormal flora intermediate (n= 50) or BV (n= 14). Patients with BV were more likely to have idiopathic infertility than women with normal vaginal flora. Patients with abnormal vaginal flora had higher mean values of IL-1β than did patients with normal vaginal flora (382 ± 361 vs. 185 ± 305; p = 0.0009, Mann-Whitney U test). Similarly, patients with abnormal vaginal flora had a higher prevalence of increased levels of IL-1β (>500pg/mL) cervical levels 15.6% (39/250) of patients with normal vaginal flora vs. 38.6% (17/44) of patients with abnormal vaginal flora; p<0.01. Patients with normal vaginal flora had a higher prevalence of low IL-1β (< 100 pg/mL) cervical levels (66.4% [166/250]) of patients with normal vaginal flora vs. 27.3% (12/44) of patients with abnormal vaginal flora; p<0.0001. Patients with abnormal vaginal flora were more likely to have elevated levels of IL-8 (68.6% [25/35]) with IL-8 > 1000 pg/mL vs. 31.44% [11/35]; p = 0.003). Increasing levels of IL-1β was associated with elevated IL-8 values (mean IL-8 concentration of 1084 pg/mL with the IL-1β <50 pg/mL; p<0.0001). No differences were found in relation to GS results and IVF outcome. In conclusion, BV may result in elaboration of IL-1β and IL-8 which can induce PTD. Treatment with tetracycline may overcome the adverse pregnancy outcome in women with BV.

RECURRENT VULVOVAGINAL CANDIDIASIS IS ASSOCIATED WITH A HIGH RATE OF CUTANEOUS IRRITANT REACTION. Summers PR and Baker J. University of Utah Medical Center, Salt Lake City, Utah.

Objective: To Determine whether recurrent vulvovaginal candidiasis (RVVC) is associated with an increased risk for irritant reaction from topical agents.

Study Design: The prevalence of irritant reaction from topical agents was determined for 57 women with RVVC, 45 women with non-yeast vaginitis, and 50 women with no history of recurrent vulvovaginitis. Analysis was by Chi-square. Effectiveness of vulvar irritant dermatitis therapy with topical oils and irritant avoidance was evaluated for 39 women with RVVC.

Results: Women with RVVC reported a 78% rate of vulvar irritant reaction, and a 52% rate of irritant reaction at other body sites. P values were <0.01 and .012 respectively in comparison with the non-yeast vaginitis group. At follow-up, 79% of 39 women with vulvar irritant dermatitis noted that continued dermatitis therapy had improved their Candida vaginitis symptoms.

Conclusions: There is an association between RVVC and cutaneous irritant reaction that may perpetuate symptoms after topical yeast therapy. Treatment of concurrent irritant dermatitis is essential.

FEMALE GENITAL TRACT BACTERIAL CO-ISOLATES WITH CANDIDA ALBICANS IN PATIENTS WITHOUT CLINICAL VAGINITIS. Monif GRG and Carlson HJ. Creighton University School of Medicine, Omaha, Nebraska.

Objective: In vitro, Candida albicans has been demonstrated to have the ability to inhibit the replications of selected bacteria. In vivo, a lack of information exists on the impact of Candida albicans on the vaginal bacterial flora. The purpose of this study is to identify the co-existing bacterial flora when Candida albicans is isolated from vaginal cultures submitted to a hospital-based testing facility for reasons other than for vulvovaginitis.

Methodology: All (240) specimens received from ambulatory care clinics over a six-month period were cultured for aerobic and anaerobic bacteria and Candida species. Those specimens submitted for cervicitis, vaginitis or vaginal discharge, and those from which yeasts other than C. albicans were isolated, were eliminated. Control for sample biases, a subgroup composed of all pregnant women, for whom cultures were done as screening procedures, was similarly studied. Chi-square analyses, comparing the prevalence of individual bacteria isolated with and without the presence of C. albicans for all study populations, were done using SPSS for Windows software (1994).

Results: Two hundred and forty consecutive specimens were bacteriologically analyzed. Of the 220 vaginal samples in the study, Candida albicans was isolated in 44 instances (20%). Neither the presence of the lactobacilli nor the presence of Gardnerella vaginalis markedly influenced the isolation rate of C. albicans. The group B streptococci had a greater probability of co-isolation when Candida albicans was present (27.3% vs 16%), but this was not statistically significant (p<0.08). Disassociation between the presence of Candida albicans and the co-isolation of the Peptostreptococcus and anaerobic gram-positive cocci and/or bacilli was noted (p<0.019). While the incidence of gram-positive aerobic bacilli was reduced 30/176 (17.1%) versus 6.44 (13.5%), this reduced incidence of recovery in the presence of Candida albicans was not statistically significant. Isolation data of the subgroup constituted by pregnant women supported these observations.

Conclusion: Within the limitations of the study, statistically, the data suggests that an inverse relationship exists between the presence of C. albicans and recovery of Peptostreptococcus and anaerobic gram-positive cocci and bacilli.

ROLE OF CYTOKINES IN A MURINE MODEL OF PRETERM LABOR INDUCED BY EXPERIMENTAL URINARY TRACT INFECTION. Kaul R, Khan S, Martens M, Crosson J, Kachroo B and Kaul A. University of Minnesota, Minneapolis Medical Research Foundation, Minneapolis, Minnesota.

Preterm birth is a major cause of perinatal morbidity and mortality. However, the etiology of preterm labor is poorly understood. Among the etiological factors of preterm birth are infections including UTIs. Recently, we developed a murine model of preterm delivery by infecting pregnant C3H/HeJ mice with Dr adhesin bearing E. coli by urethral catheterization. More than 85% of the pregnant mice infected with Dr+ E. coli deliver preterm (before Day 18 of gestation). Several reports suggest that host derived cytokines are...
important in the mechanism of preterm parturition associated with infections. The present study was conducted to understand the role of various cytokines involved in the pathophysiology of preterm births in a gestational UTI associated model of preterm labor. To identify the specific role, if any, of cytokines in gestational UTI induced preterm labor, splenocyte cultures were analyzed for the release of various cytokines and for the expression of mRNA in the kidneys and placenta of these mice. Mice splenocyte cultures were prepared from pregnant mice infected with Dr+ or Dr− E. coli or sterile PBS on Day 7 of gestation by sacrificing all the three groups of mice on Day 17 of gestation. Cytokine release for IFN-γ, IL-4, IL-10, IL-6 and TNF-α was evaluated in presence of heat killed Dr+ or Dr− bacteria or purified Dr antigen exposed for 24 hours. The cytokine mRNA in the renal and placental tissues was evaluated by using the Riboquant system (Pharmin, San Diego, California). Increased IFN-γ, TNF-α, IL-6 and IL-10 response was observed in Dr+ E. coli (mutant) infected or control pregnant animals and, thus, seem to play an important role in infection induced preterm labor. The increased cytokine mRNA for IFN-γ, TNF-α and IL-6 seen in placenta and kidneys of Dr+ E. coli infected mice further confirms the important role of these cytokines in the induction of preterm labor. The increased mRNA expression of IL-15 also observed in the placenta of Dr+ E. coli infected pregnant mice, suggests for the first time, an important role of this cytokine in infection induced preterm labor.

AN IMMEDIATE HYPERSENSITIVITY RESPONSE TO HUMAN 60kD HEAT SHOCK PROTEIN (hsp60): A POSSIBLE INFLUENCE ON RECURRENT VULVOVAGINITIS (RVV). Giraldo P*, Neuer A, Ribeiro-Filho AD, Simoes JA, Feitosa SS, Tristao A and Witkin SS. Universidade de Campinas, Sao Paulo, Brazil; Cornell University Medical College, New York, New York.

The etiology of RVV remains unclear. An underlying allergic response may increase susceptibility to contracting a symptomatic vulvovaginal infection in some women. Inflammation is associated with induction of heat shock proteins to promote cell survival and induction of chemokines to attract various lymphoid cells to the inflamed site. We investigated whether an immediate hypersensitivity response to heat shock proteins and elaboration of chemokines associated with allergic inflammation were present in some women. Serum and a vaginal wash sample were obtained in Campinas from 24 women with a history of RVV and 19 controls. All subjects were healthy and asymptomatic at the time of sampling. Samples were tested for IgE antibodies to hsp60 and the 70kD heat shock protein (hsp70), hsp60 and hsp70 antigen and vaginal samples from RVV patients (13/24, 54.2%) than controls (6/19, 31.6%) (p=0.009). The presence of vaginal hsp60 was associated with detection of hsp60 in serum (p=0.03). In all subjects examined, IgE antibodies to hsp60 were detected in 18 (41.8%) of the women tested. Its occurrence in serum was highly correlated with detection of RANTES (p 0.005), a chemoattractant for eosinophils and basophils. In contrast, only five women had IgE antibodies to hsp70, and this was not associated with RANTES. IgE anti-hsp60 was also detected more frequently in women with eotaxin (47.1% vs. 26.9%), but this did not reach statistical significance. Whether induction of hsp60 by stress or infection results in an IgE-mediated immune response and RANTES induction in some women and increases susceptibility to RVV remains to be determined.