



# 12<sup>th</sup> World Congress on Endometriosis

30 April to 3 May 2014

## Abstracts

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Wednesday 30 April 2014

PCC#5 - Light into the myth of endometriosis

PCC5-1

KEY MECHANISMS IN THE REGULATION OF ENDOMETRIOSIS

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**Introduction:** According to patients demand we have to offer different therapeutical strategies in the treatment of endometriosis.

**Study Objective:** To evaluate 3 therapy strategies: hormone therapy, surgery, and combined treatment.

**Design:** Prospective, randomized, controlled study (Canadian Task Force classification I).

**Methods:** Four hundred fifty patients with genital endometriosis, aged 18 to 44 years, before first laparoscopy. Patients were randomly assigned to 1 of 3 treatment groups: hormone therapy, surgery, or combined treatment. Patients were reevaluated at second-look laparoscopy, at 2 to 2 months after 3-month hormone therapy in groups 1 and 3 and at 5 to 6 months in group 2 (surgical treatment alone). Outcome data were focused on the endometriosis stage, recurrence of symptoms, and pregnancy rate.

**Results:** All treatment options, independent of the initial Endoscopic Endometriosis Classification stage, achieved an overall cure rate of 50%. A cure rate of 60% was achieved with the combined treatment, 55% with exclusively hormone therapy, and 50% with exclusively surgical treatment. Recurrence of symptoms was lowest in patients who received combined treatment. Significant benefit was achieved for dysmenorrhea and dyspareunia. An overall pregnancy rate of 55% to 65% was achieved, with no significant difference between the therapeutic options.

**Conclusion:** In the quest to find the most effective treatment of genital endometriosis, this clinical randomized study shows the lowest incidence of recurrence with combined surgical and medical treatment and improved pregnancy rate in any medically treated patients with or without surgery. The highest cure rate (Endoscopic Endometriosis Classification stage 0) for endometriosis was also achieved in the combined treatment group.

J Minim Invasive Gynecol. 2013 Jul – Aug; 20 (4):473-81

**Wednesday 30 April 2014**

**PCC#5 - Light into the myth of endometriosis**

**PCC5-2**

**HMG A 2 PROTEIN IS A KEY MOLECULE IN THE PATHOGENESIS OF BENIGN DISEASES AS  
ENDOMETRIOSIS AND FIBROIDS**

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Increasing experimental evidence suggests a pivotal role of adult stem cells in the pathogenesis of benign gynecological diseases and in particular endometriosis and uterine fibroids. We were able to subdivide between two main genetic subtypes in fibroids characterized by either mutations of the gene encoding mediator subcomplex 12 (*MED12*) or rearrangements of the high mobility AT-hook 2 protein gene (*HMGA2*) . Tumors of both genetic entities do not only differ by their average size but also only very rarely co-occur in one patient. Moreover, *HMGA2*-rearranged fibroids usually make their appearance as single nodules whereas those carrying *MED12* mutations are often multiple. Both mutations seem to be primary and causally linked to the disease by targeting uterine smooth muscle stem or progenitor cells. In case of *HMGA2*-rearranged fibroids it mimics a permanently activated stem cell population without hindering further differentiation. In a similar manner differently expressed patterns of *HMGA2*, and not *MED 12* mutations, account for endometrial polyps and endometriosis. The promotion of growth and development not only of fibroids but also endometriosis seems to be directed by *HMGA2* modulated self renewal of mesenchymal stem cells which is counteracted by p53 dependent apoptotic pathways.

**Wednesday 30 April 2014**

**PCC#5 - Light into the myth of endometriosis**

**PCC5-3**

**IS ADENOMYOSIS AN INDICATION OR CONTRAINDICATION FOR LAPAROSCOPIC SUBTOTAL HYSTERECTOMY?**

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In symptomatic patients with bleeding disorders and dysmenorrhea, adenomyosis is the main cause often combined with uterine myomatosis. Especially in this subgroup of young and symptomatic patients the laparoscopic subtotal hysterectomy with electric morcellation is a standard surgical method. The morcellation of the uterus means to shred a histologically unknown variety of tissues in the abdominal cavity. Several publications have shown the correlation between morcellation and postoperative peritoneal endometriosis and adenomyosis. Are we offering a really safe procedure performing a laparoscopic subtotal hysterectomy without knowing if we are morcellating adenomyosis? Do we cause peritoneal endometriosis or adenomyosis? In how many patients? Symptomatic or asymptomatic? After how many years? What does that mean for the informed consent? Do we need a presurgical histology? How can morcellation be safer? How representative is the result of a pathologic report on 500 – 2000 gr of morcellated tissue? This presentation will give some answers. Alternatives and consequences will be discussed.

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PCC#5 - Light into the myth of endometriosis

PCC5-4

IMPACT OF SURGICAL AND HORMONAL THERAPY ON ENDOMETRIOSIS

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PCC#5 - Light into the myth of endometriosis

PCC5-6

**ENDOMETRIOSIS PATIENTS IN THE POSTMENOPAUSAL PERIOD: PRE- AND POSTMENOPAUSAL FACTORS INFLUENCING POSTMENOPAUSAL HEALTH**

Dietmar Haas,<sup>1,2</sup> Peter Wurm, MD,<sup>1</sup> Wolfgang Schimetta, PhD,<sup>4</sup> Kathrin Schabetsberger, MD,<sup>1</sup> Andreas Shamiyeh, MD,<sup>3</sup> Peter Oppelt, MD,<sup>1,2</sup> and Helge Binder, MD<sup>1,2,5</sup>

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**Objective:** To evaluate patients' health status and the course of endometriosis from the premenopausal to the postmenopausal period and evaluate influencing factors that may be relevant.

**Methods:** Questionnaire completed by 35 postmenopausal women in whom endometriosis had been histologically confirmed premenopausally. Correlation and regression analyses were carried out to identify factors relevant to their postmenopausal health status.

**Results:** Overall, there was clear improvement in typical endometriosis symptoms and sexual life. Clear associations ( $P < 0.005$ ) were observed between premenopausal factors like physical limitations caused by the disease, impaired social contacts and psychological problems, and postmenopausal pain and impairment of sexual life. Three statistical models for assessing pain and impairment of sexual life in the postmenopausal period were calculated on the basis of clinical symptoms in the premenopausal period, with a very high degree of accuracy ( $P < 0.001$ ;  $R^2 = 0.833 / 0.857 / 0.931$ ).

**Conclusions:** The results of the survey strongly suggest that physical fitness and freedom from physical symptoms, a good social environment, and psychological care in both the premenopausal and postmenopausal periods lead to marked improvements in the postmenopausal period with regard to pain, dyspareunia, and influence on sexual life in endometriosis patients. Specialized rehabilitation clinics for endometriosis patients aimed at maintaining physical fitness and providing appropriate psychological care should be available and accessible.

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**PCC#5 - Light into the myth of endometriosis**

**PCC5-7**

**INFLUENCE OF ENDOMETRIOSIS ON COH AND OOCYTE QUALITY IN AN ART CYCLE**

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Impact of endometriosis on outcome of ART cycles is described for different stages of endometriosis. There is an evidence that endometriosis causes an ovulatory dysfunction and a disturbed folliculogenesis. For this reason controlled ovarian hyperstimulation (COH) and oocyte quality are discussed regarding the influence of endometriosis on them. COH is the first step in an ART procedure influencing folliculogenesis. As it was shown serum AMH level is decreased in women with endometriosis compared to a presumably healthy cohort, representing women undergoing an ART treatment for male factor only, even depending on the rAFS grade. As a result of this there is a higher requirement for gonadotropins for COH in women with endometriosis. It has also been shown that serum AMH level correlates with oocyte quality showing a decreased oocyte quality for the upper and lower percentiles for serum AMH. As a lower serum AMH level has been shown for women with endometriosis, endometriosis has to be considered as a possible parameter for the decreased oocyte quality. Physicians have to consider diagnosis for infertility, including endometriosis, for an ART treatment.

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**PCC#5 - Light into the myth of endometriosis**

**PCC5-8**

**PREGNANCY SPECIFIC FEATURES IN ENDOMETRIOSIS**

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Endometriosis is a chronic disease that affects women in their reproductive age. Main symptoms are pain and infertility issues. But what happens if patients become pregnant? Endometriosis is expected to disappear or at least shrink in size in pregnancy and thus shouldn't cause the specific pain symptoms any more.

Publications about risks for patients with endometriosis in pregnancy are rare. Large cohort studies show risks for preterm delivery, SGA, preeclampsia and stillbirth significantly associated with endometriosis. Mainly case reports exist that describe partly severe complications in pregnancy. These complications apply for all entities of endometriosis, i.e. adenomyosis, endometrioma, peritoneal endometriosis and especially deep infiltrating endometriosis.

As complications are rare and symptoms are often unspecific doctors and midwives should be aware about potential risks. They should pay special attention to unclear symptoms that can be severe and in extreme case life-threatening for the patient and the unborn child.

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**PCC#5 - Light into the myth of endometriosis**

**PCC5-10**

**CELL SURFACE RECEPTORS AS TARGETS IN ENDOMETRIOSIS**

Dr. Martin Götte<sup>1</sup>

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Current therapies for endometriosis often face the challenge of frequent recurrence, generating a need for more efficient therapies. Apart from surgical interventions, pharmacological treatment is largely based on endocrine approaches [1]. While this mode of interfering with growth of the endometriotic lesion makes sense in light of the finding that endometriosis is a hormone-dependent disease, novel treatments may be developed based on a selective targeting of cellular processes additionally contributing to its pathogenesis.

At the cellular level, proliferation, invasiveness, angiogenesis, aberrant immune cell function, and a possible involvement of adult stem cells may promote establishment and growth of the lesion at ectopic sites [2-4]. Of note, several of these processes are controlled via signal transduction processes mediated by cell surface receptors and their respective ligands. For example, receptor tyrosine kinases (RTKs) such as VEGF-receptors or the hepatocyte growth factor receptor c-Met modulate proliferation, angiogenesis and cellular invasiveness, processes known to be dysregulated in endometriosis [2,3]. Chemokine and interleukin receptors respond to the proinflammatory environment contributing to endometriosis, whereas Notch family receptors may influence the phenotype of endometriotic stem cells [2,4]. Finally, an aberrant function of cell surface proteoglycans, which act as coreceptors for all of these receptor classes apparently influences endometriotic cell behaviour [2].

As cell surface receptors represent good drug targets [5], and as several drugs initially developed for antitumoral, antiangiogenic and anti-inflammatory purposes (e.g. RTK and chemokine receptor inhibitors, gamma-secretase inhibitors) are readily available, a potential application in the context of endometriosis pharmacotherapy may be worth considering. However, potential side effects need to be carefully considered, as some effects may be still tolerable for patients in an oncological context, but may not be an option for patients suffering from a benign disease.

References:

[1] Dunselman GA et al. ESHRE guideline: management of women with endometriosis. Hum Reprod. 2014 Jan 15. [Epub ahead of print], PMID: 24435778, [2] Schneider C et al. Targeting of syndecan-1 by micro-ribonucleic acid miR-10b modulates invasiveness of endometriotic cells via dysregulation of the proteolytic milieu and interleukin-6 secretion. Fertil Steril. 2013;99:871-881.e1., [3] Rocha AL et al. Angiogenesis and endometriosis. Obstet Gynecol Int. 2013;2013:859619., [4] Götte M et al. Increased expression of the adult stem cell marker Musashi-1 in endometriosis and endometrial carcinoma. J Pathol. 2008;215:317-29, [5] Gashaw I et al. What makes a good drug target? Drug Discov Today. 2011;16:1037-43.

Thursday 1 May 2014

Seminar #1 - Genetics, epigenetics and hereditary aspects

M1-1

**LARGE-SCALE EXOME CHIP GENOTYPING REVEALS NOVEL CODING VARIATION ASSOCIATED WITH ENDOMETRIOSIS**

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**Objectives:** Genome-wide association studies (GWAS) have identified nine genetic loci harbouring common variants associated with endometriosis to date. However, these variants typically map to non-coding genomic regions, and together explain only ~3% of the estimated 52% heritability of the condition. Here, we investigate the contribution of coding variation to endometriosis pathogenesis.

**Design:** We undertook genotyping of 910 cases of European ancestry from the Oxford Endometriosis Gene (OXEGENE) study with the Illumina Exome Chip. For comparison, we utilised 13,334 population controls (including 6,828 females), also of European ancestry, from the UK Exome Chip Consortium.

**Materials and Methods:** We evaluated the association of endometriosis with: (i) individual coding variants; and (ii) “burden” of loss of function (all frequencies) and rare non-synonymous (minor allele frequency [MAF] less than 1%) variants within genes. Analyses were adjusted for two principal components to account for UK population structure.

**Results:** No individual coding variants achieved exome-wide significant evidence ( $p < 5 \times 10^{-7}$ , Bonferroni correction for 100,000 variants) of association. The strongest signals include missense variants in TAF1L (D141N,  $p = 1.5 \times 10^{-5}$ , MAF=0.077%), CDKL3 (D273N,  $p = 1.6 \times 10^{-5}$ , MAF=0.098%), and CEACAM5 (N256Y,  $p = 1.6 \times 10^{-5}$ , MAF=0.042%). We observed exome-wide significant evidence ( $p < 2.5 \times 10^{-6}$ , Bonferroni correction for 20,000 genes) of association with burden of loss of function variants in C16orf89 ( $p = 1.1 \times 10^{-6}$ ) and rare non-synonymous changes in NECAB3 ( $p = 1.7 \times 10^{-7}$ ), CEACAM5 ( $p = 2.7 \times 10^{-7}$ ), ZIM2 ( $p = 2.9 \times 10^{-7}$ ), ZNF485 ( $p = 1.1 \times 10^{-6}$ ), and RSAD2 ( $p = 2.1 \times 10^{-6}$ ). CEACAM5 encodes a glycoprotein involved in cell adhesion, has been implicated in carcinogenesis, and is a highly relevant biological candidate for endometriosis. None of the identified genes map to established endometriosis loci, providing no support for the hypothesis that rare coding variation can explain common GWAS association signals.

**Conclusion:** Our study provides preliminary novel insights into the contribution of coding variation to the genetic component of endometriosis. For validation, we will combine results from this study with Illumina Exome Chip genotyping of 368 cases and 572 controls of European ancestry from the Estonian BioBank, through single-variant and gene-based meta-analysis.

**Keywords:** Association, exome

Thursday 1 May 2014

Seminar #1 - Genetics, epigenetics and hereditary aspects

M1-2

**META-ANALYSIS OF GWAS SIGNALS FOR ENDOMETRIOSIS TO DATE: CONSISTENCY AND HETEROGENEITY ACROSS EIGHT DATASETS TOTALLING MORE THAN 11,000 CASES AND 32,000 CONTROLS**

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<sup>1</sup> University of Oxford, Oxford, United Kingdom, <sup>2</sup> QIMR Berghofer Medical Research Institute, Brisbane, Australia, <sup>3</sup> Brigham and Women's Hospital and Harvard Medical School, Boston, United States

**Objectives:** Eight genome-wide association (GWAS) and replication studies have been published to date on endometriosis from multiple populations. We investigate consistency and heterogeneity of results across all studies and their implications for improved understanding of the condition.

**Design:** Meta-analysis of four GWASs and four replication studies including a total of 11,506 cases and 32,678 controls, and of the subset of studies that investigated associations for rAFS stage III/IV (2,859 cases).

**Materials and Methods:** GWAS and replication datasets included 9,039 cases and 27,343 controls of European (Australia, Belgium, Italy, UK, US) and 2,467 cases and 5,335 controls of Japanese ancestry. Random effects models and heterogeneity statistics (I<sup>2</sup>) were used to investigate the evidence of the nine reported genome-wide significant loci, across datasets and populations.

**Results:** Meta-analysis showed that 7/9 loci had consistent directions of effect across studies and populations, and 6/9 remained genome-wide significant ( $P < 5 \times 10^{-8}$ ) including rs12700667 on chromosome 7 ( $P = 1.6 \times 10^{-9}$ ), rs7521902 in WNT4 ( $P = 1.8 \times 10^{-15}$ ), rs10859871 in VEZT ( $P = 4.7 \times 10^{-15}$ ), rs1537377 in CDKN2BAS1 ( $P = 1.5 \times 10^{-8}$ ), rs7739264 near ID4 ( $P = 6.2 \times 10^{-10}$ ) and rs13394619 in GREB1 ( $P = 4.5 \times 10^{-8}$ ). Two independent intergenic loci, rs4141819 and rs6734792 on chromosome 2, showed significant evidence of heterogeneity across datasets ( $P < 0.005$ ). All 9 loci had stronger effect sizes among stage B cases, implying that they are likely to be implicated in the development of moderate/severe, or ovarian disease. While 2/9 loci are intergenic, the remainder are in or near genes with known functions of biological relevance to endometriosis, varying from roles in developmental pathways to cellular growth/carcinogenesis, which will be discussed.

**Conclusion:** Despite reported lack of formal replication, our meta-analysis show remarkable consistency in endometriosis GWAS results across studies, with little evidence of population-based heterogeneity. However, phenotypic definitions used have been crude. Stronger associations with stage B disease observed for most loci emphasize the importance for future studies to include detailed sub-phenotypes.

**Keywords:** meta-analysis, GWAS, heterogeneity

Thursday 1 May 2014

Seminar #1 - Genetics, epigenetics and hereditary aspects

M1-3

THE PREVALENCE AND HERITABILITY OF ENDOMETRIOSIS AMONG 28 825 SWEDISH TWINS

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**Objectives:** To study the prevalence of endometriosis and to test a hypothesized genetic component in a large population based Swedish twin cohort.

**Design:** A cross-sectional large population-based twin cohort study.

**Materials and Methods:** The data consisted of two compiled surveys conducted by the Swedish Twin Registry, and the data obtained from the National Inpatient Registry. Endometriosis diagnosis was validated with medical records. Proband-wise concordances and within-pair correlations were calculated. Quantitative genetic model-fitting methods were used to investigate the heritability of endometriosis.

**Results:** 28 825 female twins were included in this study comprised of 3 595 monozygotic and 3 601 dizygotic complete pairs. The prevalence of endometriosis was 5.6%. Endometriosis diagnosis was validated in 67.4% of cases. The proband-wise concordance for endometriosis was higher in monozygotic (0.21) than in dizygotic twin pairs 0.12, indicating a genetic effect. Similarly the within-pair correlation for monozygotic (0.44) was higher than for dizygotic twins (0.21). Quantitative genetic modeling showed that a model including additive genetic (A) and unique environmental (E) factors provided the most parsimonious fit. In the AE model, 43% (95% confidence interval 35-51%) of the variance in liability to endometriosis is attributed to additive genetic factors with the remaining 57% (95% confidence interval 50-65%) to unique environmental effects.

**Conclusion:** The prevalence of endometriosis was somewhat lower in this population based twin cohort compared with previously published data from more selected groups of women. Both additive genetic and unique environmental factors seem to explain the variation in susceptibility to endometriosis.

**Keywords:** Endometriosis, prevalence, heritability

Thursday 1 May 2014

Seminar #1 - Genetics, epigenetics and hereditary aspects

M1-4

**GENOMIC REARRANGEMENTS (COPY NUMBER VARIANTS) MAY PLAY A ROLE IN THE PATHOGENESIS OF ENDOMETRIOSIS.**

Hans Albertsen<sup>1</sup>, Rakesh Chettier<sup>1</sup>, Kenneth Ward<sup>1</sup>

<sup>1</sup>Juneau Biosciences, LLC, Salt Lake City, United States

**Objectives:** To identify Copy Number Variations (CNVs) that contributes to the genetic risk for developing endometriosis.

**Design:** Our study-design employs high-density SNP genotyping arrays to screen a large and well-characterized Case-Control population for CNVs associated with endometriosis. Patients were recruited via Juneau's outreach program.

**Materials and Methods:** The study includes 2,434 surgically confirmed endometriosis cases and 17,053 population controls of European descent. Samples were genotyped using the Illumina Human OmniExpress array with stringent quality filters. PennCNV and a Circular Binary Segmentation (CBS) algorithm were used to determine copy-number. ParseCNV was used to screen for regional copy-number association.

**Results:** We identified 13 independent rare CNV regions (CNVRs) each spanning 10 or more SNP probes associated with Endometriosis at a nominal significance threshold p-value of 0.05 using either PennCNV or CBS. (3.5% of the cases and 1.1% of population controls had one of these CNVs. All CNVRs passed visual inspection using the Log R Ratio and B Allele Frequency plots. Of these, 12 are deletions and 1 is a duplication. Three CNVRs pass the standard threshold ( $p < 5 \times 10^{-4}$ ) for CNVs. One CNVR on chromosome 7 [8,827,959-8,856,074] lies near the NXPH1 (Neurexophilin 1) gene. NXPH1 variants have been implicated as risk factors of breast and ovarian cancer. For NXPH1, we observed two homozygous and three heterozygous deletions in cases, while controls only showed six heterozygous deletions.

**Conclusion:** Novel rare CNVRs associated with Endometriosis were identified using the genotyping microarray platform. These rare CNVRs may play an important role in the pathogenesis of endometriosis. Together with the common SNPs and rare Exome variants, these CNVRs will help explain the heritability of endometriosis.

**Keywords:** CNV, GWAS, Case-Control

Thursday 1 May 2014

Seminar #1 - Genetics, epigenetics and hereditary aspects

M1-5

**A SEARCH FOR SOMATIC MUTATIONS IN DEEP INFILTRATING ENDOMETRIOSIS USING EXOME SEQUENCING.**

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**Objectives:** To search for somatic point mutations in the ectopic endometrium in patients with deep infiltrating endometriosis using next generation sequencing. The hypothesis is that somatic mutations in endometriotic cells are the cause of the abnormal invasive growth properties.

**Design:** As a pilot study we collected four different tissues (ectopic and eutopic endometrium, neighboring unaffected tissue, and wholeblood) from patients (n=3) with deep infiltrating endometriosis. Exome Sequencing was performed on DNA from the lesion and the neighboring tissue to identify genetic differences, representing potential somatic point mutations in the lesion.

**Materials and Methods:** DNA extraction and exome sequencing was performed at Aros Biotechnology (Århus, Denmark) using Agilent SureSelect at an average coverage of 30x. Sequence alignment was performed using GATK. Variant calling was performed using the software MuTect, developed for detection of low frequency mutations in cancer samples.

**Results:** In the three patients, we found in total 9 genetic differences between lesion and paired normal unaffected tissue, representing 9 potential somatic point mutations. All changes passed our stringent filtering criteria's including a coverage threshold of 20x in both normal sample and lesion and a minimum of 4 reads representing the alternative allele in the lesion. In one patient, a somatic mutation was identified in CDC42, a gene that is in part regulated by estrogen and that has been shown to be associated with endometriosis in a large meta analysis of genome wide association studies. Other genes with potential mutations included DHRS4 and PRDM15. Pyrosequence validation for each somatic mutation are ongoing, to exclude potential technical artifacts introduced during library preparation.

**Conclusion:** Our data suggest that rare somatic mutations may be found in the ectopic lesion in deep infiltrating endometriosis. Pending validation, these mutations may provide clues to the underlying disease mechanism. Our study demonstrate that inclusion of a paired normal sample is instrumental for detection of somatic events.

**Keywords:** Exome-sequencing, somatic mutation

Thursday 1 May 2014

Seminar #2 - Adenomyosis

M2-1

**PALE CELLS DIAPEDESIS IN THE ENDOMETRIAL-MYOMETRIAL JUNCTIONAL ZONE. NEW INSIGHT ON ADENOMYOSIS PATHOGENESIS**

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**Objectives:** Ultrastructural study of the junctional zone (JZ) in adenomyosis (AM), to elucidate the enigma of the pathogenesis of AM and to search for microtrauma evidence in the JZ.

**Design:** Twenty-four uteri from premenopausal women underwent laparoscopically-assisted vaginal hysterectomy were included and assigned to AM group (12 uteri) and non-AM group (n=12). Biopsies were obtained from the JZ of the anterior, posterior and fundus of the uterus at the midline, being the most prevalent sites of AM occurrence.

**Materials and Methods:** The JZ biopsies at the fundo-cornual raphe were studied using the transmission electron microscopy (TEM) and stained with van Gieson stain for collagen fibers. In addition, immunohistochemistry staining for E-cadherin, Transforming Growth Factor Beta Receptors (TGFβR) 1, 2 and 3 were performed.

**Results:** TEM could show the so-named Pale cells, found eccentrically in the basal endometrial glands of AM. In different stages (partial/total detachment-thinning out-early diapedesis-late diapedesis), we could document different localisation of the Pale cells inside and outside the basal glands. They lacked desmosomal connection to the neighbouring epithelial cells. Ultramicrorupture of the basal lamina of these glands opposing these cells and abnormal nuclear infolding of the glandular epithelial cells were evident. The inner myometrial muscle fibers lost their parallelism, mimicking the outer myometrium in AM. No significant difference in E-cadherin, TGFβR1 or 2 expressions between both groups could be detected. Only TGFβR3 was significantly higher expressed in AM than non-AM.

**Conclusion:** Pale cells are speculated to be endometrial epithelial stem cells which can actively migrate into the myometrium - eased by lack of desmosomes - where they transform into AM, in a process might be mediated by TGFβR3. Ultramicrorupture at the JZ in AM is evident.

**Keywords:** Adenomyosis, Junctional zone

Thursday 1 May 2014

Seminar #2 - Adenomyosis

M2-2

**RADIOFREQUENCY THERMAL ABLATION FOR SYMPTOMATIC UTERINE FOCAL ADENOMYOSIS - PROSPECTIVE PRELIMINARY EXPERIENCE.**

Colette Campana<sup>1</sup>, Stefano Scarperi<sup>2</sup>, Giovanni Pontrelli<sup>2</sup>, Marcello Ceccaroni<sup>3</sup>, Alfredo Ercoli<sup>4</sup>, Valentino Bergamini<sup>5</sup>

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**Objectives:** To evaluate the feasibility and efficacy of laparoscopic radiofrequency thermal ablation of uterine symptomatic focal adenomyosis.

**Design:** Prospective cohort preliminary study. Setting: four hospitals in Italy.

**Materials and Methods:** Fifteen women with symptomatic uterine focal adenomyosis underwent radiofrequency thermal ablation under laparoscopic guidance. Gynecological examination and ultrasound evaluation of adenomyosis volume were performed at the baseline and at the postoperative follow-up at 3, 6, 9, 12 months. The impact of adenomyosis related symptoms was assessed using Visual Analogic Scale.

**Results:** The median number of adenomyosis localization treated per patient was one (1-2). The median baseline volume of the adenomyosis was 60 cm<sup>3</sup> (18-128). The median reduction in adenomyosis volume was 32%, 49.4%, 59.6% and 65.4% at 3, 6, 9, and 12 months, follow-up evaluation, respectively. A significant progressive improvement in the symptoms score was observed at three, six, nine, and 12 months follow-up.

**Conclusion:** In this pilot study, laparoscopic radiofrequency thermal ablation successfully reduced adenomyosis-related symptoms and volume, appearing as a valuable alternative to major surgery, with significant symptoms relief.

**Keywords:** Adenomyosis radiofrequency ablation

Thursday 1 May 2014

Seminar #2 - Adenomyosis

M2-3

**INVOLVEMENT OF HGF-INDUCED EPITHELIAL-MESENCHYMAL TRANSITION IN ADENOMYOSIS**

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**Objectives:** The exact mechanism of gland invagination into myometrium in women with adenomyosis is still unclear. Involvement of estrogen-induced epithelial-mesenchymal transition (EMT) in cancer metastasis has been reported. As an estromedin growth factor, here we investigated the possible role of hepatocyte growth factor (HGF) in EMT in women with adenomyosis.

**Design:** This is a case-controlled biological research with prospective collection of full thickness biopsy specimens from endometrium to myometrium after hysterectomy from 15 women with adenomyosis and 12 women without adenomyosis and their retrospective evaluation. Endometrial epithelial cells (EECs) and myometrial smooth muscle cells (SMCs) were isolated in primary culture.

**Materials and Methods:** The associations between HGF and E-cadherin/N-cadherin/Vimentin in endometrium and in EECs were examined by immunohistochemistry and RT-PCR. Effect of HGF on morphological change of EECs and in EECs migration was examined. Expression of transcriptional repressors of E-cadherin, SLUG and SLAIN, in response to HGF/estrogen was examined by RT-PCR.

**Results:** : HGF was able to scatter both EECs and SMCs. Higher E-cadherin gene expression achieved with confluent EECs was abrogated after application of HGF (50, 100ng/ml) with up-regulation of N-cadherin. An inverse association between HGF and E-cadherin expression was observed in gland cells of the basalis endometrium derived from women with adenomyosis. This effect was not observed in functionalis endometrium. A 48hr exposure to HGF (100ng/ml) changed phenotype of EECs into mesenchymal phenotype and induced migration of EECs as confirmed by Boyden's chamber assay. In addition to individual effect of estrogen (E2) and HGF, an additive effect between them was observed in the up-regulation of SLUG and SLAIN gene in Ishikawa cells. This effect corresponded to inverse protein expression of SLUG and E-cadherin.

**Conclusion:** Our findings suggest that HGF-induced EMT may be involved in gland invagination deep into myometrium in women with adenomyosis. This effect of HGF in inducing EMT may be supported by local estrogen. Further studies are needed to strengthen our current findings.

**Keywords:** adenomyosis, HGF, EMT

Thursday 1 May 2014

Seminar #2 - Adenomyosis

M2-4

**LAPAROSCOPIC RADIOFREQUENCY THERMAL ABLATION: A NEW APPROACH TO SYMPTOMATIC UTERINE FOCAL ADENOMYOSIS.**

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**Design:** Prospective cohort preliminary study. Setting: four hospitals in Italy.

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**Conclusion:** In this pilot study, laparoscopic radiofrequency thermal ablation successfully reduced adenomyosis-related symptoms and volume, appearing as a valuable alternative to major surgery, with significant symptoms relief.

**Keywords:** Adenomyosis radiofrequency ablation

Thursday 1 May 2014

Seminar #2 - Adenomyosis

M2-5

**THE EFFICACY OF INTRA-VAGINAL DANAZOL SUPPOSITORY THERAPY FOR INFERTILE WOMEN WITH ADENOMYOSIS.**

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**Objectives:** Adenomyosis could be a cause of infertility. Medical therapies with GnRH agonist or danazol are clinically used to alleviate pain symptom but efficacy on infertility is questionable and their side-effects are worrisome. Local vaginal suppository therapy with danazol can be an alternative option while maintaining ovarian functions in these women.

**Design:** Intra-vaginal danazol suppository was prescribed to infertile women with adenomyosis and they were prospectively followed-up at university hospital.

**Materials and Methods:** Eighteen women with overt adenomyosis, had failed standard infertility therapy including surgical reduction and IVF-ET, were enrolled. Danazol intra-vaginal suppository was prepared as in-house prescription kneading 100mg oral tablet with base and used daily. Clinical backgrounds of women, type of adenomyosis (focal or diffuse), and reproductive outcomes were evaluated.

**Results:** Mean age of the subjects was 37.7±3.7 years. Half of the subjects were nulligravida. Adenomyosis were diagnosed by MRI as diffuse (n=3), anterior wall focal (n=9) and posterior wall focal (n=6). Co-existing endometriosis was found in 14 women (78%). Three women had received reduction surgery o before intra-vaginal treatment. Self-reported alleviation of pain symptom was notified. Five women (27.8%) conceived with IVF-ET and one woman (5.6%) conceived spontaneously after intra-vaginal danazol therapy. Three pregnancies resulted in miscarriage.

**Conclusion:** Intra-Vaginal danazol suppository therapy can be considered as an adjuvant medical therapy for infertile women with adenomyosis who suffer from repeated pregnancy failure.

**Keywords:** Adenomyosis infertility danazol

Thursday 1 May 2014

Seminar #3 - Immunology and stem cells

M3-1

**SOLUBLE MICA (MAJOR HISTOCOMPATIBILITY CLASS I-RELATED CHAIN A): A POSSIBLE INVOLVEMENT IN THE PATHOGENESIS OF ENDOMETRIOSIS**

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**Objectives:** MICA, a stress inducible molecule, is released as soluble proteins down-modulating NKG2D receptor expression on CD8+  $\alpha\beta$ T and NK cells leading to a diminished cytotoxic response. The aim of this study is to evaluate the presence of soluble MICA in women with endometriosis and to compare it to healthy controls.

**Design:** A case-control study to compare women with endometriosis and without endometriosis (control group).

**Materials and Methods:** One hundred thirty women with endometriosis confirmed by videolaparoscopy and histology of biopsies and 35 women undergoing laparoscopy for tubal ligation, without endometriosis were enrolled in this study. Serum and peritoneal fluid levels of sMICA were determined by ELISA (R&DSystems) (limit of detection= 31pg/mL). Statistical analysis: Mann–Whitney test.

**Results:** Our results showed higher sMICA levels in the peritoneal fluid (median=61,50pg/mL, range 31-843; mean=124.50,  $\pm$ 151.00) when compared to serum levels (median=<31pg/mL, range <31-155; mean=42.46,  $\pm$  25.53) in endometriosis patients ( $p < 0.0001$ ). Soluble MICA levels in peritoneal fluid of controls were also higher when compared to its serum levels ( $p= 0.0009$ ). The comparison between sMICA serum levels between patients and controls showed increased levels in women with endometriosis ( $p= 0.0028$ ). The same was observed for sMICA in peritoneal fluid ( $p= 0.0060$ ). The highest sMICA levels in serum and peritoneal fluid were detected especially in severe stages of the disease (III and IV) when compared with control group (serum,  $p=0,0006$ ; peritoneal fluid,  $p=0,0046$ ).

**Conclusion:** Our results indicate increased levels of sMICA in endometriosis patients, particularly in the peritoneal fluid. This may be secondary to the presence of an inflammatory environment, contributing to the reduction of the cytotoxic activity of NK and CD8+ T cells thus facilitating the implantation and growth of endometrial tissue.

**Keywords:** sMICA; NK; endometriosis

Thursday 1 May 2014

Seminar #3 - Immunology and stem cells

M3-2

**RETROGRADE MENSTRUATION OF ENDOMETRIAL STEM/PROGENITOR CELLS IN WOMEN WITH ENDOMETRIOSIS**

Caroline Gargett<sup>1</sup>, Hirotaka Masuda<sup>1</sup>, Kijana Schwab<sup>1</sup>, Charmaine Tan<sup>1</sup>, Gareth Weston<sup>2</sup>

<sup>1</sup>The Ritchie Centre, Monash Institute of Medical Research, Melbourne, Australia, <sup>2</sup>Department of Obstetrics & Gynaecology, Monash University, Melbourne, Australia

**Objectives:** To determine whether endometrial stem/progenitor cells play a role in the pathogenesis of endometriosis using newly identified markers for human endometrial mesenchymal stem cells (eMSC) and epithelial progenitor cells (eEPC). Specifically, to determine if endometrial stem/progenitor cells are shed by retrograde menstruation into the pelvic cavity in women with endometriosis.

**Design:** Cycling women undergoing laparoscopy for suspected endometriosis (n=14) or tubal ligation (controls, n=13) on day two of their menstrual period were recruited and samples of uterine menstrual blood (UMB), peritoneal fluid (PF) and peripheral blood (PB) were collected. Endometriosis was diagnosed and scored at surgery according to AFS guidelines.

**Materials and Methods:** UMB was collected using soft tubing inserted into the uterine cavity. PF was collected via the laparoscope before other procedures. Single cell suspensions were obtained, leukocytes removed by CD45 magnetic beads, cell cloning done, and flow cytometry used to quantify the concentration of eMSC (W5C5+ cells) and eEPCs (marker+ cells).

**Results:** In menstrual blood, there was no difference in the concentration of clonogenic cells between endometriosis and control samples (3,100 CFU/mL n=6 vs 47 CFU/mL n=9 respectively; P=0.58). Similarly the concentration of W5C5+ eMSCs (126,000/mL in endometriosis vs 21,600/mL in controls; each n=7, p=0.13) and marker+ eEPCs (82,500/mL in endometriosis vs 149,000/mL in control; each n=4, p=0.48) did not differ. No W5C5+ eMSCs or marker+ eEPCs were found in peripheral blood from either group. While the volume of peritoneal fluid was similar from women with and without endometriosis, the concentration of viable cells (P<0.005), W5C5+ eMSCs (344,000/mL in endometriosis vs 77/mL in controls; each n=7, P<0.001) and marker+ eEPCs (13,000/mL in endometriosis vs 1,050/mL in controls; each n=4, P<0.03) was significantly elevated in the endometriosis group.

**Conclusion:** Our data suggest that there may be preferential retrograde shedding of endometrial stem/progenitor cells into the pelvic cavity during menstruation in women with endometriosis compared to controls. These stem/progenitor cells may have greater ability to survive in the peritoneal fluid of women with endometriosis, enabling them to initiate endometriosis lesions.

**Keywords:** Stem cells, menstruation

Thursday 1 May 2014

Seminar #3 - Immunology and stem cells

M3-3

**DYSFUNCTIONAL UTERINE NATURAL KILLER (UNK) CELL DEVELOPMENT IN ENDOMETRIOSIS**

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**Objectives:** The objective of this study was to explore the hypothesis that the differentiation of uNK cells was abnormal in women with endometriosis.

**Design:** Analysis of progenitor uNK cells was performed in eutopic endometrial biopsies obtained from consenting women undergoing laparoscopy. Patients were classified as having endometriosis, AFS stage I-II (n=13), III-IV (n=8) or normal pelvis (n=9). Growth factors critical for NK development, IL-15 and stem cell factor (SCF) were also studied.

**Materials and Methods:** The numbers and phenotypes of uNKs, stained with CD45, CD56, CD3, and CD16, were defined using flow cytometry with antibodies for different stages of NK development: CD10, CD34, CD94, CD117, CD161, integrin $\beta$ 7, and Nkp46. Levels of IL-15 and stem cell factor (SCF) were analysed using qRT-PCR, protein array and ELISAs.

**Results:** UNK (CD45+CD56+CD3-) numbers were higher in women with stages I-II (mean: 6.0%) and stages III-IV (mean: 10.1%) endometriosis when compared with unaffected women (mean: 2.1%). UNK progenitors (CD45+CD56+CD3-CD34+) were also higher in women with endometriosis (mean: stages I-II: 35.3%, stages III-IV: 33.4%, normal: 23.0%). UNKs in intermediate stages of development were also increased in women with endometriosis, characterised by expression of integrin $\beta$ 7 (mean: stages I-II: 90.5%, stages III-IV: 85.4%, normal: 72.3%) and CD117 (mean: stages I-II: 46.8%, stages III-IV: 41.5%, normal: 9.0%). Additionally, the soluble ligands, IL-15 and SCF (ligand for CD117) required for NK development are reduced in women with stages I-II endometriosis and further reduced in stages III-IV endometriosis. All of these changes were evident across all stages of the menstrual cycle.

**Conclusion:** This study shows for the first time that altered uNK maturation, as evidenced by an accumulation of excess progenitor cells and abnormal levels of significant growth factors, may lead to compromised function underpinning the aetiology of endometriosis. This data also supports dysfunctional uNK development as an explanation for endometriosis-related infertility.

**Keywords:** Progenitor natural killer

Thursday 1 May 2014

Seminar #3 - Immunology and stem cells

M3-4

**NOTCH INHIBITION REDUCES REDUCES STEMNESS VIA ALTERED EXPRESSION OF SOX2, LIFR AND PODXL IN AN ENDOMETRIOTIC CELL LINE**

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**Objectives:** A dysregulated stem cell function has been implicated in the pathogenesis of endometriosis. Here, we investigate the effects of notch pathway inhibition via gamma secretase inhibitors (GSI) on stemness-associated properties of the epithelial endometriotic cell line 12Z.

**Design:** 12Z cells were subjected to siRNA knockdown of the notch pathway regulators MSI1 and MSI2, or GSI treatment, followed by analysis of stemness-related marker expression.

**Materials and Methods:** 12Z cells were subjected to gamma secretase inhibitor treatment or MSI1/MSI2 siRNA treatment and analyzed for changes in gene expression by TaqMan low density arrays and qPCR. The impact of notch pathway inhibition on stem cell properties was investigated by flow cytometric aldehyde dehydrogenase activity assays.

**Results:** GSI treatment led to a reduction of ALDH+ cells, reduced cell viability in MTT assays, and increased apoptosis. TaqMan Low density array analysis followed by qPCR confirmation revealed a significant downregulation of the pluripotency-associated transcription factor SOX2, previously shown to be associated with endometriosis of the LIF receptor, IFITM1, a regulator of primordial germ cell function, and the stemness-associated factor PODXL. Expression of Msi1 and the notch antagonist numb was upregulated by GSI, while treatment of 12Z cells with recombinant notch-1 induced transcriptional downregulation of Msi1, numb, DLL1 and DLL4.

**Conclusion:** Our preclinical data suggest that pharmacological interference with the notch signaling pathway may be a worthwhile approach in the treatment of endometriosis that warrants further investigation.

**Keywords:** Notch, gamma-secretase-inhibitor, Musashi

Thursday 1 May 2014

Seminar #3 - Immunology and stem cells

M3-5

**REPEATED OBSERVATION OF AN ASSOCIATION BETWEEN ELEVATED PERITONEAL INFLAMMATORY CYTOKINES AND SEVERE DYSMENORRHEA AMONG WOMEN WITH ENDOMETRIOSIS**

Michael Beste<sup>1</sup>, Marta Privato<sup>2</sup>, Douglas Lauffenburger<sup>1</sup>, Mauricio Abrão<sup>2</sup>, Keith Isaacson<sup>3</sup>, Linda Griffith<sup>1</sup>

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**Objectives:** Pain and infertility exhibit limited concordance with the extent of endometriotic disease observed at the time of diagnosis. We examined whether peritoneal fluid inflammatory factors were more strongly indicative of concurrent symptom severity and evaluated the reproducibility of our findings in two independent clinical populations.

**Design:** Cross-sectional study of two patient populations (n=41; n=47) from independent academic medical centers presenting with laparoscopically diagnosed endometriosis.

**Materials and Methods:** Severity of pelvic pain and reproductive history were documented at the time of surgery by standardized questionnaires. Concentrations of fifty cytokines in peritoneal fluid aspirates were determined via multiplex immunoassay. Statistical associations between cytokine levels, lesion characteristics, and symptomatology were evaluated by univariate analysis and multivariate regression.

**Results:** Multivariate analysis revealed a significant proportional association between inflammatory cytokine abundance and severity of dysmenorrhea in both patient populations (P = 0.0338 and P = 0.0277, respectively). Cytokines associated with increased menstrual pain in each cohort included IL-1 $\beta$ , IL-1ra, IL-6, IL-8, IL-10, RANTES, MIF, MCP-1, G-CSF, HGF, and GRO $\alpha$  (FDR<0.05). In comparison to morphologic evaluation, cytokine status was more discriminating of cyclic pain than disease staging alone; OR = 6.29 (95% CI 1.30-30.3) vs. OR = 1.83 (95% CI 0.54-6.10), respectively. Deep dyspareunia and non-cyclic pelvic pain were not associated with cytokine abundance or a unique lesion distribution in either cohort. Fertility performance was likewise unrelated to increased cytokine levels or affected tissue sites.

**Conclusion:** Increased levels of soluble inflammatory cytokines within the peritoneal fluid are directly associated with severe dysmenorrhea among women with endometriosis. Our findings support the role of local immune-mediated activity as a causative or exacerbating factor contributing to cyclic pelvic pain, independent of total disease burden.

**Keywords:** Dysmenorrhea; Inflammation; Cytokines

Thursday 1 May 2014

Seminar #4 - Endometrioma and ovarian reserve

M4-1

**IRON AVAILABILITY IS INCREASED IN INDIVIDUAL HUMAN OVARIAN FOLLICLES IN CLOSE PROXIMITY TO AN ENDOMETRIOMA.**

Paola Panina<sup>1</sup>, Ana Maria Sanchez<sup>1</sup>, Enrico Papaleo<sup>1</sup>, Sonia Levi<sup>1</sup>, Paola Viganò<sup>1</sup>, Massimo Candiani<sup>1</sup>

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**Objectives:** To investigate whether the iron content of an endometrioma represents a potential source of toxicity for the adjacent follicles.

**Design:** Experimental study on 13 women with unilateral endometrioma at the time of the IVF treatment. Follicular fluid from individual follicles, proximal and distal to the endometrioma, and from the contralateral ovary were retrieved by transvaginal aspiration.

**Materials and Methods:** Iron and H/L ferritin were measured in individual follicles by specific ELISAs. The expression of transferrin receptor (TfR1) and H ferritin in granulosa cells from individual follicles were evaluated by RT-PCR. Analysis of the number of oocytes retrieved and embryo quality after IVF was also performed.

**Results:** Total iron concentration was higher in endometrioma-proximal follicles compared to distal ones ( $p=0.009$ ). L ferritin was higher in proximal vs distal follicles or follicles from the healthy ovary ( $p=0.04$  and  $p=0.03$  respectively). H ferritin was higher in the proximal and distal follicles compared with follicles in healthy ovary ( $p=0.04$  and  $p=0.01$  respectively). H ferritin transcripts in granulosa cells were higher in proximal vs follicles from healthy ovary ( $p=0.02$ ). TfR1 transcripts were higher in proximal vs distal follicles ( $p=0.03$ ). The number of oocytes retrieved in proximal was lower than in distal follicles ( $p=0.001$ ).

**Conclusion:** These data indicate that the elevated iron content in the endometrioma affects iron availability in proximal follicles leading to impaired follicle development.

**Keywords:** Endometrioma, iron, ferritin

Thursday 1 May 2014

Seminar #4 - Endometrioma and ovarian reserve

M4-2

**HYDRODISSECTION WITH DILUTED PITUITRIN FOR LAPAROSCOPIC CYSTECTOMY OF OVARIAN ENDOMETRIOMA: A TECHNIQUE TO REDUCE DAMAGE TO OVARIAN RESERVE**

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**Objectives:** To assess the efficacy and effects on ovarian reserve of a new surgical technique, hydrodissection with diluted pituitrin, for laparoscopic cystectomy of ovarian endometrioma.

**Design:** The patients diagnosed as ovarian endometrioma were randomly divided into 2 groups to undergo laparoscopic cystectomy: (1) Study group (32 cases): the operation was performed using hydrodissection with diluted pituitrin, and (2) Control group (30 cases): Conventional surgery was performed without use of pituitrin.

**Materials and Methods:** The operation time and blood loss were compared between 2 groups. Furthermore, for study group cases with bilateral endometriomas we measured anti-Mullerian hormone (AMH), follicle stimulating hormone (FSH), estradiol and antral follicle count (AFC) on Day 2 of menstrual cycle preoperatively, and 1, 6 and 12 months after surgery, respectively.

**Results:** The operation time and blood loss of the study group operated with hydrodissection with diluted pituitrin were significantly reduced, compared with those of control cases ( $P < 0.05$ ). For further study to assess the effects of hydrodissection excision on ovarian reserve, the measurements of the levels of AMH, FSH, E2 and the number of AFC did not show significant changes before and after the operation in the study group cases with bilateral endometriomas.

**Conclusion:** Hydrodissection with diluted pituitrin is an efficient technique to effectively decrease the blood loss and shorten the operation time when performing laparoscopic cystectomy. Our data suggest that this surgical method may become a useful alternative of cystectomy in considering protection of ovarian reserve for the patients with ovarian endometrioma.

**Keywords:** Ovarian reserve; hydrodissection;

Thursday 1 May 2014

Seminar #4 - Endometrioma and ovarian reserve

M4-3

**VARIATION OF AMH LEVEL FOLLOWING ENDOMETRIOMA ABLATION USING PLASMA ENERGY**

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**Objectives:** To assess the postoperative ovarian reserve in women managed for unilateral endometriomas by PlasmaJet ablation/vaporization.

**Design:** Prospective pilote study without control group.

**Materials and Methods:** 25 women with unilateral ovarian endometriomas and no ovarian surgery antecedents, were enrolled from November 2010 to November 2012. They underwent complete vaporization of endometriomas using the PlasmaJet. They had AMH level assessment preoperatively, 3 months after the surgery and at the end of the follow up (April To August 2013).

**Results:** The age was 30.4±4.6 years, 60% were nulligesta and 12% homosexual. Preoperative infertility care was recorded in 40%. When compared to preoperative value, the 3 months postoperatively AMH level decreased by 39%. In seven patients the preoperative value was inferior to 2 ng/mL. The mean follow up, from the day of the surgery to the last visit was 18 months (SD 8 months, range 7 to 29 months). When compared to the AMH value at 3 months, we recorded a mean increase of the AMH level of 32%, which corresponds to an average of 0.6 ng/mL (–1.7 to 4.6 ng/mL). 15 women had a normal level of the AMH (>2 ng/mL). Among women intending to be pregnant, 50% became pregnant during the follow up.

**Conclusion:** PlasmaJet ablation of endometriomas is followed by significant variations in the AMH level, suggesting that the assessment 3 months after the surgery does not reflect the actual impact of the surgery on the ovarian reserve.

**Keywords:** Endometrioma; ablation; vaporization;

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Seminar #4 - Endometrioma and ovarian reserve

M4-4

**RECURRENCE OF OVARIAN ENDOMETRIOMA AFTER LAPAROSCOPIC EXCISION**

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**Objectives:** Analyse factors that might influence the recurrence after ovarian endometrioma laparoscopic excision.

**Design:** Retrospective cohort study. We evaluated 202 cases of ovarian endometrioma after laparoscopic excision, followed between 2003- 2012. A minimum of two years postoperative follow-up after the surgery was made.

**Materials and Methods:** Chosen recurrence criteria was suggestive ultrasound finding, repeated at 3, 6 and 12 months, and subsequently once a year. Factors were analyzed using chi-squared, student T test or Fisher test and logistic regression model for multivariable hazards. The significance level for inclusion in the model was 5%.

**Results:** The overall rate of recurrence was 16,4%. Demographics data as age, race, presenting symptoms, smoking, physical exercise habits, parity and surgical procedure techniques didn't show statistical significance for recurrence rate of ovarian endometrioma. Using multivariate proportional hazards regression analysis we observed that cyst diameter larger than 6cm ( $p= 0,013$ ; OR 4,65 ; 95%CI= 1,38- 15,69) and postoperative medical treatment discontinuity ( $p< 0,001$ ; OR 57,84 ; 95%CI= 7,08- 472,39) were significantly associated with major recurrence rates.

**Conclusion:** Endometrioma larger than 6cm and hormonal treatment interruption were associated with higher ovarian endometrioma recurrence rates after laparoscopic treatment.

**Keywords:** Endometrioma, recurrence, laparoscopy

Thursday 1 May 2014

Seminar #4 - Endometrioma and ovarian reserve

M4-5

**PRIMORDIAL FOLLICLE LOSS AFTER ENDOMETRIOMA CAPSULE STRIPPING IN LAPAROSCOPIC SURGERY**

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**Objectives:** Ovarian endometrioma is characterized by cystic formation filled by chocolate-like content with a fibrous wall. The treatment includes stripping the capsule preserving ovarian tissue by laparoscopic technique. The objective of this study was to evaluate (quantitatively) the number of primordial follicles lost after stripping the endometrioma capsule in laparoscopic surgery.

**Design:** It was performed a prospective study.

**Materials and Methods:** The study was performed from 2004 to 2013 in a tertiary hospital. Patients with endometriosis that were submitted to laparoscopic surgery were invited to participate. The cyst capsule was stripped avoiding the use of bipolar electrocautery. The capsules were analysed at pathology lab for microscopic count of the primordial follicle.

**Results:** Forty nine endometriomas capsules were included from 41 women (8 of them had bilateral cysts). The mean age was 35 years old. The mean number of primordial follicles lost that were found in the capsule was 17,3. In 14 cases, none follicles were found in the capsule tissue. The highest number of follicles found was 186 primordial follicles. There was no statistical difference but there was a trend to significancy towards an inverse relation between age and number of follicles removed (older patients had a smaller loss of follicles). There was also a trend to significancy comparing the number of follicles lost and size of the capsule (bigger capsule showed bigger loss).

**Conclusion:** The primordial follicle loss after removing endometrioma capsule seems not to be numerically significant to impair the ovarian reserve.

**Keywords:** Endometrioma, follicles, reserve.

Thursday 1 May 2014

Session - Surgical treatment

S1-1

**COLORECTAL RESECTION VERSUS RECTAL CONSERVATIVE SURGERY IN THE MANAGEMENT OF RECTAL ENDOMETRIOSIS: PRELIMINARY RESULTS OF ENDORE RANDOMIZED TRIAL**

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**Objectives:** To determine whether performing colorectal resection is responsible for a higher rate of postoperative digestive and urinary dysfunction and an increased risk of postoperative complications when compared to rectal nodules excision (shaving or disc excision) through a randomized trial (ENDORE, NCT 01291576).

**Design:** Prospective in intention to treat randomized trial, enrolling patients with deep endometriosis infiltrating the rectum up to 15 cm from the anus, for whom rectal involvement exceeds 20 mm on length, the muscular layer on depth, and <50% on rectal circumference. Randomization between colorectal resection and conservative procedures.

**Materials and Methods:** Main outcome : at least one postoperative complaint at 24 months, among severe constipation, defecation pain, frequent bowel movements, anal incontinence and de novo dysuria. Standardized gastrointestinal questionnaires were filled preoperatively and at each postoperative visits (at 6, 12, 18 and 24 months). Thirty patients were required in each arm.

**Results:** We analyzed 50 women managed in Rouen from 03/2011 to 05/2013 with postoperative follow up > 3 months. Among the 25 patients enrolled in the arm 1, 10 underwent rectal shaving, 13 disc excision, while 2 patients (8%) had a colorectal resection. The diameter of the disc was 49±12 mm. In women managed by colorectal resection in the second arm, the length of the segment removed (mm) was 92±45, and the height of the colorectal anastomosis (mm from the anus) was 82±42. Women managed by conservative surgery had a significantly lower risk of Clavien 3a complications, and a slightly decreased risk of Clavien 3b complications. Despite the incomplete follow up, the rate of pregnancies among women intending to get pregnant is 67% vs. 46% (P=0.42).

**Conclusion:** Conservative surgery may be performed instead colorectal resection in 92% of rectal endometriosis with rectal involvement >20 mm, with a decrease of the risk of some postoperative complications. As regards the main outcome, full results will be available in 2016.

**Keywords:** Rectal endometriosis; shaving

Thursday 1 May 2014

Session - Surgical treatment

S1-2

**EARLY RISE IN SERUM C-REACTIVE PROTEIN INDICATES SUBSEQUENT SURGICAL COMPLICATION AFTER LOW ANTERIOR RESECTION FOR RECTO-SIGMOID ENDOMETRIOSIS**

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**Objectives:** Recto-sigmoid endometriosis is the most advanced and surgically challenging form of the disease. The aim of this study was to demonstrate the potential value of serial measurements of serum C-reactive protein (CRP) and white blood cell count (WBC) after laparoscopic low anterior resection for deep endometriosis with bowel involvement.

**Design:** Recto-sigmoid endometriosis should be treated by the laparoscopic approach but controversy remains whether to perform shaving/discoid excision or segmental bowel resection. Anastomotic leakage and ureteral injury are feared complications, and early diagnosis is crucial. Measurement of CRP and WBC are used as indicators of such problems in rectal cancer surgery.

**Materials and Methods:** One-hundred-and-five patients who underwent laparoscopic anterior resection for recto-sigmoid endometriosis were monitored daily by serum CRP and white blood cell count (WBC) until discharge from the hospital. Patients with anastomotic leakage or ureteral injury (group A; n=23) were compared to patients without these complications (group B; n=82).

**Results:** The daily average values of serum CRP were significantly higher in group A starting at the 2nd post-operative day (POD 2, p = 0.004). A cut-off value of 60 mg/L on POD 3 resulted in a sensitivity (78%) and specificity (67%) of CRP in assessing the risk of leakage. A decrease in CRP from POD 1 to POD 3 predicted uncomplicated course in 92.0% of the cases. Postoperative WBC values did not display any significant differences between the two groups.

**Conclusion:** An early rise in CRP was a strong indicator of a severe surgical complication. Monitoring of CRP for early detection of anastomotic leakage or ureteral injury is recommended.

**Keywords:** Recto-sigmoid endometriosis crp

Thursday 1 May 2014

Session - Surgical treatment

S1-3

**SURGICAL MANAGEMENT OF ENDOMETRIOMAS ON IN VITRO FERTILIZATION OUTCOMES: A SYSTEMATIC REVIEW AND META-ANALYSIS**

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**Objectives:** Surgical management of endometriomas in infertile women prior to in vitro fertilization (IVF) is controversial. Recent evidence indicates that surgical manipulation may impede ovarian response and decrease IVF success.

**Design:** A systematic review and meta-analysis.

**Materials and Methods:** We searched MEDLINE, EMBASE and the Cochrane Library (inception to September 2013) for studies comparing fertility outcomes in women with endometriomas undergoing surgical and conservative treatment. Study selection, data extraction and quality assessment were conducted independently by 2 reviewers. The meta-analysis was carried out using a random effects model.

**Results:** Eleven studies (1 randomized trial and 10 observational studies; 2,996 women) meeting the inclusion criteria were identified. Across studies, there were similar pregnancy rates between the surgery and non-intervention groups (risk ratio [RR] = 0.91; 95% CI = 0.54 to 1.54 in the randomized trial; RR = 1.10; 95% CI = 0.90 to 1.33 in observational studies). Similar number of oocytes was retrieved in the surgical group as compared to the conservatively managed group (mean difference [MD] = -0.48; 95% CI = -1.07 to 0.11).

**Conclusion:** Our systematic review suggests that surgical management of endometriomas prior to IVF treatment yields similar clinical outcomes as conservative management. Well-designed and powered trials are needed to determine if there is any clinical advantage to surgical management of endometriomas prior to IVF.

**Keywords:** Cystectomy, endometriomas, in-vitro-fertilization

Thursday 1 May 2014

Session - Surgical treatment

S1-4

**NERVE-SPARING LAPAROSCOPIC ERADICATION OF DEEP ENDOMETRIOSIS WITH SEGMENTAL RECTAL AND PARAMETRIAL RESECTION: THE NEGRAR METHOD. A PROSPECTIVE STUDY ON 331 PATIENTS.**

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**Objectives:** To compare effects of a nerve-sparing laparoscopic approach to endometriosis excision with parametrial and bowel resection and the “classical technique” in terms of bladder, colo-rectal and sexual dysfunctions.

**Design:** Single centre, prospective comparative study.

**Materials and Methods:** All patients underwent laparoscopic excision of deep endometriosis with segmental bowel resection. Two different techniques were adopted: the “classical” approach and the “Negrar Method” (nerve-sparing technique). A Questionnaire about Quality of Lives, sexual, colo-rectal and urinary functions was administered at a mean time of 24.8 months.

**Results:** 331 patients were included in the present series. 163 patients received a nerve-sparing radical excision of pelvic endometriosis with segmental bowel resection (group A), whereas 168 patients were treated with the classical technique (group B). Intra, peri and post-operative complications were similar in the two groups. Mean operating time was significantly lower in Group B when compared with Group A (301.5 mins VS 351.8 mins); ( $p < 0.01$ ). The mean days of self-catheterization was significantly lower in nerve-sparing Group (39.8 days) when compared to the non nerve-nerve sparing Group (121.1 days), ( $p < 0.001$ ). Relapse rate within 12 months after surgery was comparable between two groups. Patients of Group A suffered more frequently from urinary retention between 1 and 6 months ( $p = 0.035$ ) compared with Group B ( $p = 0.018$ ).

**Conclusion:** Our laparoscopic nerve-sparing complete excision of endometriosis seems to be feasible and, as reported in our recent study, offers good results in terms of bladder morbidity reduction with apparently higher satisfaction than classical technique.

**Keywords:** Bowel, laparoscopy, nerves

**Thursday 1 May 2014**  
**Session - Surgical treatment**

S1-5

**PARTIAL RESECTION OF THE EXTRASEROSAL PELVIC FASCIA IS A CRUCIAL SURGICAL STEP IN THE MANAGEMENT OF PATIENTS WITH COLORECTAL ENDOMETRIOSIS**

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**Objectives:** Extraserosal pelvic fascia (EPF) is a connective tissue containing vessels and nerve branches of the pelvic organs between the visceral and the parietal pelvic fascia. The objectives were to describe the characteristics of patients with EPF infiltration, and to assess the impact of its resection in patients with colorectal endometriosis.

**Design:** A prospective cohort study including all patients who underwent segmental colorectal resection for symptomatic deep infiltrative endometriosis (DIE) in our center between January 2001 and December 2011, has been conducted.

**Materials and Methods:** We defined the involvement of the EPF as the need to perform an uncrossing manoeuvre between the ureter and the uterine artery to laterally remove the infiltrated EPF (i.e. parametrectomy) and, to dorsally remove the infiltrated pararectal portion of the EPF.

**Results:** During the study period, 227 patients had colorectal segmental resection for DIE. Out of the 112 patients (49.4%) who required EPF resection, 63 (56%) had unilateral and 49 (44%) bilateral EPF resection. Patients requiring EPF resection had a higher total American Society for Reproductive Medicine score ( $p=0.0004$ ), more associated resected DIE lesions ( $p<0.0001$ ) and longer surgery ( $p<0.0001$ ). Patients with associated EPF resection more frequently required blood transfusion ( $p=0.003$ ), were more likely to experience intraoperative complications ( $p=0.01$ ) and postoperative voiding dysfunction ( $p=0.04$ ). No difference in surgical characteristics, peri and postoperative morbidity was found between patients with uni or bilateral EPF resection.

**Conclusion:** EPF infiltration in patients with colorectal endometriosis reflects the severity of the disease and its removal impacts on intraoperative morbidity and leads to a higher rate of voiding dysfunction. EPF's involvement should be systematically evaluated before surgery to better inform patients about their specific risks and adapt surgical management accordingly.

**Keywords:** Colorectal endometriosis

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Session - Surgical treatment

S1-6

**LAPAROSCOPIC MANAGEMENT OF DEEPLY INFILTRATING ENDOMETRIOSIS: A COHORT PROSPECTIVE STUDY WITH 10-YEAR FOLLOW UP**

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**Objectives:** Deeply invasive endometriosis (DIE) is recognized as a special entity responsible for pain symptoms. The aim of this study is to investigate effect of conservative laparoscopic surgery with long term follow up.

**Design:** A prospective and 10 year follow-up cohort study began from 2003.

**Materials and Methods:** There are totally 580 cases of deeply infiltrating endometriosis (DIE) patients and 1000 cases of non-DIE patients pathologically diagnosed were enrolled. Clinical datas of symptoms, operation finding, laparoscopically surgery, medication, pain relief time and relapse rate post-operation were analyzed.

**Results:** The risk of pain symptoms in DIE patients were significantly increased. The OR for dysmenorrhea, CPP, deep dyspareunia, dyschezia were 6.73, 1.90, 3.09 and 4.903 respectively. The highest incidence of deep dyspareunia was observed in fornix invaded group (72.2%). The longest operative duration ( $82.00 \pm 30.58$ min) and the postoperative hospitalization ( $7.67 \pm 2.08$  days) were observed in rectum invaded group. The median pain relief time was 65 months in the patients with complete excision of DIE lesions, which was significantly longer than that in patients with incomplete excision (25 months). The rate of complication was 2.05%, including one case of colon fistula and relapse rate was 27.6% (at 5-year), 38.5% (at 10-years). Mutivariate analysis demonstrated that only incomplete excision of DIE lesions was a risk factor for shorter pain relief time.

**Conclusion:** Conservative laparoscopic surgery may effectively treat pain s in DIE patients. The systematisation of strategy is essential to make surgery more reproducible, safer. And patients could gain better life quality after conservative surgery combine with medication. Incomplete excision of DIE lesions was the significant predictor of shorter pain relief time.

**Keywords:** Laparoscopy, endometriosis, pain

**Thursday 1 May 2014**  
**Session - Surgical treatment**

**S1-7**

**LAPAROSCOPIC NEUROLYSIS FOR DEEP ENDOMETRIOSIS INFILTRATING PELVIC WALL AND SOMATIC NERVES: A RETROSPECTIVE STUDY ON 216 PATIENTS**

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**Objectives:** Objective of the present study is to review efficacy and feasibility of laparoscopic neurolysis for cases of endometriosis involving sacral plexus and/or somatic nerves causing ano-genital pain.

**Design:** Retrospective case-series, single-centre, single-surgeon study on 216 patients. In a 4-year period, we treated by laparoscopic neurolysis of sacral roots and somatic nerves 216 patients with deep infiltrating endometriosis complaining of recurrent sciatica and ano-genital pain in addition to “usual” endometriosis symptoms (i.e. dysmenorrhea, dyspareunia, dysketia) .

**Materials and Methods:** Depending from the grade of infiltration, either decompression (resection of disease up to the parietal fascia covering the nerve) or neurolysis (resection of disease together with the affected fascia covering the nerve and with perineural planes and neural fibers) was performed.

**Results:** In all of the patients a surgical whole decompression of nervous structures was performed, where in 41 (18.9%) cases a complete neurolysis was required. Complete relief from neurologic symptoms was achieved in all patients at 6 month after surgery. Neuritis was reported in 42 patients (19.4%) and successfully treated with corticosteroids and pregabalin.

**Conclusion:** Laparoscopic transperitoneal retroperitoneal nerve-sparing approach to the pelvic wall (the Possover Operation) proved to be a feasible and useful procedure even if limited to referred laparoscopic centers and anatomically experienced and skilled surgeons.

**Keywords:** Neurolysis, pain, sciatica

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Session - Infertility and ART

S2-1

**IN VITRO FERTILIZATION (IVF) EMBRYO IMPLANTATION IS NOT IMPAIRED BY  
ENDOMETRIOSIS**

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**Objectives:** to analyse ovarian response, oocytes quality and embryo implantation among IVF patients with and without endometriosis

**Design:** retrospective analysis of IVF patterns on prospectively recorded data among 1615 patients less than 35 for their first IVF attempts and comparison according to endometriosis or not, ovarian response and embryo quality. A success is defined as a delivery. 291 endometriosis cases were compared to 1316 control cases

**Materials and Methods:** the comparison includes the number of recovered oocytes, the ratio of good response ( $\geq 5$  oocytes), the embryo quality ( $\geq 2$  top quality embryos). As Single Embryo Transfer was often used, we have calculated the delivery rate with fresh embryo (FDR) and the cumulative (fresh and frozen) delivery rate (CIDR)

**Results:** In the complete group the only differences are the number of recovered oocytes (8.31 versus 10.34- $p < 0.001$ ) and the number of cycles with frozen embryos (46.7% versus 54.3 %- $p < 0.01$ ). In the endometriosis group, the good stimulation response rate (68 % versus 78%,  $p < 0.001$ ) and the good stimulation response and high embryo quality rate (36.8% versus 43.6%,  $p = 0.03$ ) was lower. In the group with a good stimulation response and high embryo quality rate for which a Single Embryo Transfer was performed, the FDR (43% versus 34.5%  $p = 0.1$ ) and the CIDR (52.3 % versus 45.8 %,  $p = 0.22$ ) were non significantly higher among endometriosis patients. No difference was found in relation with the endometriosis stage

**Conclusion:** despite numerous studies that have demonstrated endometrial abnormalities that are claimed to impair embryonic implantation, this study demonstrates that there is no reduction of the implantation ability during IVF cycles. The embryo quality is not affected but the ovarian response to hyperstimulation regimen is lower in case of endometriosis.

**Keywords:** endometriosis, IVF, implantation

Thursday 1 May 2014

Session - Infertility and ART

S2-2

**EFFECT OF INDUCED PERITONEAL ENDOMETRIOSIS ON OOCYTE AND EMBRYO QUALITY IN A MOUSE MODEL**

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**Objectives:** The aim was to assess oocyte and embryo quality in a mouse model of surgically induced endometriosis.

**Design:** This was a cross sectional – control versus treatment study in a mouse model of endometriosis. Four weeks after surgery, metaphase II (MII) oocyte and embryo quality was assessed in 33 female B6CBA/F1 mice: 17 with surgically induced endometriosis versus 16 sham-operated mice.

**Materials and Methods:** Peritoneal endometriotic lesions were surgically induced by uterine tissue transplantation into the abdominal cavity of mice. Sham-operated mice were used as control. Four weeks after surgery, mice were superovulated and mated or not in order to collect E0.5 embryos or MII oocytes. Zygote and gamete quality was assessed by immunostaining.

**Results:** In the endometriotic group (n=17), lesions had developed and adhesions were noted. Histology showed cysts surrounded by endometrial tissue. Endometriotic mice (n=6) and sham-operated mice (n=5) had similar mean number of MII oocytes (30.2 vs. 32.6) and lower proportion of normal oocytes (61.2 % vs 83.1 %). Abnormalities were over-represented in endometriotic mice oocytes: first polar body was either not totally expelled (7% vs 3%), or divided (9% vs 3%); oocytes were activated (14% vs 8%) or displayed spindle abnormalities (9% vs 3%): scattered chromosomes or arciform spindle. Endometriotic mice (n=11) had fewer zygotes per mouse than sham-operated mice (n=11) (21.0 vs 35.5) and no difference was seen concerning quality.

**Conclusion:** We found that fertility was impaired in the mouse model of surgically induced endometriosis and that a limitant step in endometriosis-associated fertility was oocyte quality. Mouse model is a promising model to better understand mechanisms of infertility in endometriosis and to assess the effect of treatments on fertility outcomes.

**Keywords:** Endometriosis, oocyte, spindle

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Session - Infertility and ART

S2-3

**EXTERNAL VALIDATION OF THE ENDOMETRIOSIS FERTILITY INDEX IN A FRENCH POPULATION. TOWARDS INDIVIDUALIZED MANAGEMENT OF INFERTILE ENDOMETRIOTIC PATIENTS?**

Christophe Poncelet<sup>1</sup>, Jeremy Boujenah<sup>1</sup>, Claire Bonneau<sup>1</sup>, Christophe Sifer<sup>1</sup>, Jean-Noel Hugues<sup>1</sup>

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**Objectives:** The aims of the study were: (i) to show an external validation of the EFI; and (ii) to observe cumulated pregnancy rates after infertility management combining surgery and Assisted Reproductive Technologies (ART)

**Design:** Observational study from January 2004 to December 2012 in a French University ART center.

**Materials and Methods:** 417 infertile and endometriotic patients after laparoscopic surgery were included. Semen analysis of couples were normal according to WHO. Spontaneous pregnancy, and cumulated (spontaneous & ART) pregnancy rates were calculated using life table analysis at 12 months regarding EFI scores. Good prognostic factors after surgery for spontaneous pregnancy were explored

**Results:** A significant relationship between EFI scores and spontaneous pregnancy rates was observed at 12 months ( $p=0.001$ ). Least function score and complete removal of endometriotic lesions and pelvic adhesions were significantly associated with spontaneous pregnancy ( $p=0,04$ ). Cumulated pregnancy rates at 18 months were 78.8%. ART benefits for pregnancy rates were more accurate for poor EFI scores.

**Conclusion:** an external validation of the EFI in a French population was demonstrated. Combining, whilst opposing, surgery for endometriosis and ART leads to 78.8% pregnancy rate at 18 months

**Keywords:** EFI, surgery, Pregnancy

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S2-4

**THE IVF-LUBE TRIAL: LIPIODOL UTERINE BATHING EFFECT FOR ENHANCING THE RESULTS OF IN VITRO FERTILISATION, A PILOT RANDOMISED TRIAL**

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**Objectives:** Preliminary data suggest Lipiodol enhances fertility through an endometrial bathing effect, much more dramatically fertility in women with endometriosis compared to unexplained infertility without endometriosis.<sup>1</sup> This trial aims to determine whether positive effects exist for those undergoing IVF/ICSI in women with a diagnosis of endometriosis or recurrent implantation failure.

**Design:** A pilot open parallel-group randomised controlled trial is currently underway and due to complete recruitment by January 2014, aiming to randomise 80 women.

**Materials and Methods:** Participants were randomised to receive a Lipiodol hysterosalpingogram or no intervention on the cycle prior to IVF/ICSI. The primary outcome measure was live birth, with secondary outcome measures including biochemical and clinical pregnancy, pregnancy loss, ectopic pregnancy, multiple pregnancy and adverse events.

**Results:** The complete data from the pilot trial will be available in January 2014. An interim analysis of the first 38 women randomised revealed a clinical pregnancy rate of 6/16 (37.5%) from IVF/ICSI with 2 additional pregnancies within the six months post-randomisation (total pregnancy rate 8/16, 50%) and live birth rate of 7/16 (43.8%) from Lipiodol followed by IVF/ICSI; versus clinical pregnancy rate 8/22 (36.4%) from IVF/ICSI with no additional pregnancies within six months post-randomisation (total pregnancy rate 8/22, 36.4%) and live birth rate 5/22 (22.7%) from IVF/ICSI alone.

**Conclusion:** Interim data show a trend towards increased live birth rates amongst women with endometriosis or recurrent implantation failure who undergo Lipiodol prior to IVF/ICSI. The completed pilot trial may provide a rationale for a new treatment approach or a platform for a larger trial.

**Keywords:** IVF/ICSI, Lipiodol, Fertility

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S2-5

**MATERNAL PERITONEAL FLUID SPHINGOLIPIDS IN ENDOMETRIOSIS-ASSOCIATED INFERTILITY**

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**Objectives:** Studies where peritoneal fluid from endometriotic women were transferred to healthy animal models showed decreased reduced embryo implantation rates, suggesting key maternal peritoneal factors in inducing endometriosis-associated infertility. However, the identity of these factors is unknown. Our aim is to clarify the role of peritoneal fluid sphingolipids in endometriosis-associated infertility.

**Design:** From 64 enrolled patients, after excluding for male infertility causes, 48 women were included for this study. Peritoneal fluid from 15 fertile (8 with endometriosis and 7 without) and 33 infertile women (21 with endometriosis and 12 without) were collected during laparoscopy.

**Materials and Methods:** Advanced liquid chromatography-mass spectrometric methods were deployed to measure more than 80 peritoneal fluid sphingolipids in a single assay. False discovery rate were kept at less than 15% to identify true significant sphingolipids. Two-way ANOVA was used to test for interactions between endometriosis and infertility.

**Results:** Using advanced mass spectrometry, we were able to identify and quantify unambiguously more than 80 sphingolipids simultaneously. False positives were controlled via adjusted p-values. With these methods, we found elevated peritoneal fluid glucosylceramides in infertile endometriotic women relative to infertile controls, congruent with the mitogenic properties of glucosylceramides. There were no significantly abundant sphingolipids between fertile controls and women with endometriosis. Importantly, comparing fertile controls versus infertile endometriotic women using Two-way ANOVA, our analysis revealed 50% to more than 130% higher concentrations of specific species of peritoneal fluid ceramide-1-phosphates, ceramides and lactosylceramides, indicating the interaction of endometriosis and infertility on these sphingolipids. In addition, the significance of these sphingolipids increased with severe endometriosis.

**Conclusion:** In this study we provide the first clinical evidence that the PF infertile women with endometriosis contain higher amounts of embryotoxic sphingolipids that may also induce defective implantation, and in turn, contributing to infertility. Understanding the underlying altered sphingolipid metabolism and managing it may significantly improve endometriosis-associated infertility.

**Keywords:** Infertility, sphingolipids, translational

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Session - Infertility and ART

S2-6

**PATIENT SATISFACTION CONCERNING ASSISTED REPRODUCTIVE TECHNOLOGY TREATMENT IN MODERATE TO SEVERE ENDOMETRIOSIS**

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**Objectives:** This study examined patient satisfaction scores concerning a single Assisted Reproductive Technology (ART) treatment cycle in moderate to severe endometriosis.

**Design:** A prospective cohort study was established from May 2012 - September 2013. Patients with surgically proven endometriosis American Society for Reproductive Medicine (ASRM) stage III-IV receiving intrauterine insemination (IUI), in vitro fertilization (IVF) or IVF preceded by long term pituitary down-regulation with a GnRH-agonist (IVF-ultralong) were asked to participate.

**Materials and Methods:** Primary outcome was patient satisfaction concerning one ART treatment cycle. Possible confounders, as endometriosis complaints, quality-of-life and treatment outcomes, were evaluated. Secondary outcome was satisfaction concerning preceding long term pituitary down-regulation. A power calculation showed that 22 patients per group were needed to show a clinically relevant difference in satisfaction.

**Results:** 25 patients were included per group; 6 patients were lost to follow up. The median patient satisfaction scores were 8.3, 7.9 and 8.0 in patients who received IUI (n=22), IVF (n=24) and IVF-ultralong (n=23), respectively (p=0.89). Both deterioration in pain and EHP-30 pain scores could not be identified as determinants of decreased patient satisfaction scores. Patient satisfaction scores were higher in women who received their first treatment attempt (p=0.002), after treatment accomplishment (p=0.04) and after a positive pregnancy test (p=0.04).

Although the median patient satisfaction score concerning preceding long term pituitary down-regulation was 6.1 (IVF-ultralong n=25, IUI n=8), only three patients would refrain from this preceding therapy in a next ART treatment attempt.

**Conclusion:** Patient satisfaction scores were not different between IUI, IVF and IVF-ultralong and were not influenced by deterioration in endometriosis complaints or quality of life. Despite low satisfaction concerning preceding long term pituitary down-regulation, most patients were motivated to use this preceding therapy in a next treatment attempt.

**Keywords:** Patient satisfaction, Quality-of-life, Pain

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S2-7

**PERITONEAL ENDOMETRIOSIS AND ALLELIC FREQUENCY OF GDF-9 (RS254285, RS254286, RS10491279), ANTI-MULLERIAN HORMONE AND RECEPTOR (AMHR2) GENES SINGLE NUCLEOTIDES POLYMORPHISMS (SNP).**

Emily De Conto<sup>1</sup>, Úrsula Matte<sup>2</sup>, Vanessa Genro<sup>1</sup>, Carlos Augusto Bastos De Souza<sup>2</sup>, João Sabino Lahorgue Cunha-Filho<sup>1</sup>

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**Objectives:** The aim of the present study is evaluate if there is a correlation among several SNP of GDF-9, anti-mullerian hormone and receptor (AMHR2) with peritoneal endometriosis. Those genes were associated to oocyte/follicle development and ovarian reserve tests.

**Design:** A case-control study was performed including 50 infertile patients with endometriosis and 50 fertile subjects submitted to laparoscopy for tubal ligation as a control group. Exclusion criteria included: autoimmune disease, coexistence of other causes of infertility, deep or ovarian endometriosis, and clinical evidence of hypogonadism, amenorrhea, or irregular cycles.

**Materials and Methods:** Blood samples were collected in EDTA tubes through venipuncture, and DNA was extracted with a commercial kit. Amplification was performed in a Veriti thermal cycler at an annealing temperature of 62°C, using 20 pmol of each primer, 0.5 U Taq DNA Polymerase, 2 mmol/L dNTP, and 1.5 mmol/L MgCl<sub>2</sub> (Invitrogen).

**Results:** Age was similar between the groups (33.5 x 33.9, P> 0.05). Moreover, FSH and TSH were also not different between cases and controls (P> 0.05). The allelic frequency of GDF-9 between cases and controls showed a significance level of P=0.433 for rs254285; P=0.129 for rs254286 and P=0.794 for rs254286. In addition, the allelic frequency of AMH receptor was not different (P=0.140). However, there is a trend for SNP allelic frequency for AMH (P=0.096). All suited SNP were in Hardy-Weinberg equilibrium.

**Conclusion:** The present study did not show difference in allelic frequency of GDF-9 SNP or AMH receptor in infertile patients with endometriosis. However, we demonstrated a trend to allelic SNP difference regarding the AMH. This report opens a new evidence in terms of endometriosis physiopathogenesis and ovulatory disorders in this disease.

**Keywords:** Endometriosis, infertility, polymorphisms

Thursday 1 May 2014

Session - Pathogenesis / aetiology

S3-1

**INTRA-TISSUE ESTRADIOL, PROGESTERONE AND TESTOSTERONE CONCENTRATIONS IN ENDOMETRIOSIS ARE IMBALANCED BY LOCAL STEROID METABOLISM**

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**Objectives:** Altered estradiol and progesterone signaling promote growth of endometriosis. Changes in the expression of steroid synthesizing genes have been reported, while the intra-tissue concentrations of the steroid hormones within the endometrium or endometriosis lesions remain unknown. We evaluated local steroid concentrations in the endometrium and different types of endometriosis lesions.

**Design:** We used LC-MS/MS to measure the intra-tissue concentrations of steroids throughout the synthesis pathway from pregnenolone to estradiol in the endometrium, and in peritoneal, ovarian and deep endometriosis lesions. Expression of steroid metabolizing and steroid target genes were also evaluated and correlated with the steroid concentrations.

**Materials and Methods:** Patients with endometriosis (n=60) and healthy controls (n=16). Serum and tissue concentrations of pregnenolone, 17-hydroxy-pregnenolone, progesterone (P4), 17-hydroxy-progesterone, DHEA, androstenedione (A4), testosterone (T), estrone, and estradiol were measured using LC-MS/MS. The expression of steroidogenic enzymes was evaluated with qRT-PCR and immunohistochemistry.

**Results:** In the control and patient endometrium, P4 concentrations reflected the cyclic systemic P4 levels. However, no cycle dependent changes in P4 concentration were observed within endometriosis lesions. We have earlier reported similar loss of cyclical changes and elevated tissue concentrations of estradiol in endometriosis. Moreover, remarkably high intra-tissue T concentrations were measured in endometriosis, being 3- 37- times higher as compared with the corresponding serum levels depending of the lesion type and cycle phase, the difference being highest in peritoneal endometriosis. Also mRNA expression of several androgen dependent genes was altered in endometriosis further suggesting intra-tissue hyperandrogenemia. Among the steroid metabolizing genes HSD3B2 was most constantly elevated and its inhibition reduced A4 production in primary endometriotic cell culture.

**Conclusion:** Local steroid metabolism determines the intra-tissue sex steroid concentrations both in the endometrium and endometriosis. Elevated E2, P4, and T concentrations without cycle dependent changes alter the intra-tissue steroid environment that is critical for disease pathogenesis. This underlines the importance of local regulation of steroid metabolism in treatment of endometriosis

**Keywords:** Progesterone, testosterone, metabolism

Thursday 1 May 2014

Session - Pathogenesis / aetiology

S3-2

**FETAL AND POSTNATAL DEVELOPMENTAL ANOMALIES AFTER EXPOSURE TO ENDOMETRIOSIS IN UTERO AFFECTING TWO GENERATIONS**

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**Objectives:** Determine mechanisms by which exposure to endometriosis in utero causes developmental anomalies in fetuses and offspring across generations such that treatments may be developed to restore fertility or alleviate infertility

**Design:** A well-established multigenerational model for endometriosis routinely performed in our laboratory was used. Gestational day 15 (d15) fetuses and postnatal offspring from F0 mothers which had endometriosis or sham surgeries, their F1 daughters (exposed to endometriosis as embryos) and their F2 granddaughters (exposed to endometriosis as germ cells) were analyzed.

**Materials and Methods:** Differences in fetus/pup and spontaneous loss numbers and gender ratio were determined by One-Way ANOVA. Differences in AGD, birth weight and weight gain PD 5–22 were calculated by Two-Way ANOVA (Endo/Sham mother, gender) and Bonferroni testing. Eye opening and sexual maturation were tested by Chi2. P <0.05 was significant.

**Results:** From the F0 Endo lineage, the most noteworthy anomalies were 1) fewer, smaller and less viable d15 fetuses and 2) reduced body weight and delayed sexual maturity in both F1 and F2 female (detected by vaginal opening) and male (detected testis descent into scrotum and weight) by pups compared to progeny of the F0 Sham rats within generation. Examples of other phenotypic abnormalities found in F1 fetuses and pups of F0 Endo mothers were observed in the placental decidua, time of eye opening and postnatal pup weight gain. Dystocia and postpartum cannibalization were also found only in F0 mothers with endometriosis compared to controls.

**Conclusion:** Embryo and embryonic germ cell exposure to endometriosis in utero cause fetal and postnatal phenotypic and reproductive anomalies compared to controls providing insight into mechanisms underlying multigenerational endometriosis subfertility. Such discoveries represent prime targets for development of revolutionizing therapies addressing the cause or prevention of subfertility in women with endometriosis.

**Keywords:** Infertility, exposure, generational

Thursday 1 May 2014

Session - Pathogenesis / aetiology

S3-3

**METABOLIC REPROGRAMMING OF THE PERITONEAL MESOTHELIUM BY TGF- $\beta$  MAY PROMOTE ENDOMETRIOSIS LESION DEVELOPMENT**

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**Objectives:** TGF- $\beta$  induces the Warburg-effect, which is the metabolic conversion of glucose to lactate in normoxia in the stroma surrounding tumours. Overexpression of energy-rich lactate ‘feeds’ tumours and fuels their progression. As TGF- $\beta$  is increased in the peritoneum of women with endometriosis we asked, is there a Warburg-like effect in endometriosis?

**Design:** Ex vivo analysis of peritoneal biopsies and peritoneal fluid collected from women with and without endometriosis. In vitro analysis of human primary peritoneal mesothelial cells (PMC), and an immortalized mesothelial cell line (MeT-5A).

**Materials and Methods:** Lactate and TGF- $\beta$ 1 concentrations in peritoneal fluid were measured by colorimetric assay and ELISA (n=18). Glycolysis enzymes were studied in peritoneal biopsies by qRT-PCR and immunochemistry (n=16). The effect of TGF- $\beta$ 1 on enzyme expression and lactate production was assessed in PMC and MeT-5A cells (n=3-6) by qRT-PCR and western blot

**Results:** Peritoneal fluid of women with endometriosis had higher concentrations of TGF- $\beta$ 1 (p<0.05) and lactate (p<0.05), compared to healthy controls, and these elevated levels were significantly correlated with each other (p<0.05). The metabolic driver hypoxia inducible factor-1 $\alpha$  (HIF-1 $\alpha$ ) was expressed in peritoneal biopsies and was localized to the PMC. Exposure of PMC and MeT-5A cells to TGF- $\beta$ 1 increased expression of lactate (p<0.05) without observed changes in cytotoxicity. TGF- $\beta$ 1 exposure induced stable expression of the HIF-1 $\alpha$  protein and significantly increased HIF-1 $\alpha$  gene expression in PMC (p<0.05) and MeT5a cells (p<0.05). HIF-1 $\alpha$  target genes involved in glycolysis; GLUT-1 (p<0.05), LDHA (p<0.05) and PDK-1 (p<0.05), were all significantly increased on exposure to TGF- $\beta$ 1.

**Conclusion:** We have shown that lactate is significantly increased in the peritoneum of women with endometriosis and this is associated with TGF- $\beta$ 1 and glycolysis enzyme expression. These results suggest a change in the metabolic phenotype of the PMC in women with endometriosis, similar to the Warburg effect described in tumorigenesis.

**Keywords:** TGF- $\beta$ 1 Peritoneum Metabolism

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Session - Pathogenesis / aetiology

S3-4

**LOCALIZATION OF CELLULAR INTERACTIONS AND NEUROANGIOGENESIS IN DEEPLY INVASIVE ENDOMETRIOSIS IMPLICATES IMPORTANT ROLE OF MACROPHAGE INFILTRATION**

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**Objectives:** Objective: To understand the etiology of pelvic pain in deeply invasive endometriosis (DIE), molecular histology methods were used to characterize neurovascular growth in DIE lesions.

**Design:** Design: A case series of 12 DIE lesion biopsies was collected. The anatomic distribution of the DIE lesions included uterosacral (n=3), paravaginal (n=3) and rectovaginal septum (n=3) implants. Serial sections from paraffin blocks were cut, decloaked, blocked and prepared for immunohistochemistry (IHC) using routine methods as summarized below.

**Materials and Methods:** Methods: Following optimization of specific antibodies, IHC was performed on 8 micron paraffin sections to localize cell types and their secretory products in situ. Serial sections of DIE lesions allowed proteins to be anatomically co-localized. Alkaline phosphatase conjugated secondary antibodies were labeled with Vector Red as the chromogen.

**Results:** Results: As predicted by the severe pain symptoms associated with DIE, these lesions demonstrated high density sensory nerves decorated with PGP9.5, neuron specific enolase and  $\beta$ -tubulin antibodies. The nerves were closely associated with CD34-positive microvessels that penetrated the fibrotic stroma of the DIE implants. CD68-positive macrophages infiltrated the DIE stroma and encircled endometriotic glands, but were not noted in the striated muscle surrounding the lesions. NF- $\kappa$ B p65 subunit proteins were prominent in the invading macrophages and in DIE epithelium, where they revealed a predominantly nuclear localization. Brain-derived neurotrophic factor (BDNF) was highly concentrated within glands and stroma of the DIE lesions, in close proximity to small nerves and capillaries. In some cases, BDNF was observed to be localized in the lesion microvasculature itself.

**Conclusion:** The findings provide in situ data supporting our theory that endometriosis provokes a neuroangiogenic response via the production of BDNF and other paracrine factors (Asante & Taylor, 2011). New evidence that NF- $\kappa$ B-expressing macrophages are associated with neuroangiogenesis predicts that inflammatory mediators modulate BDNF expression. This hypothesis is under investigation presently.

**Keywords:** Deeply invasive endometriosis

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Session - Pathogenesis / aetiology

S3-5

**ENDOMETRIOSIS AND HIGH RISK OF COMORBIDITIES: ANALYSIS OF MORE THAN HALF MILLION PATIENTS**

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**Objectives:** We hypothesize that long term oxidative-inflammatory endometriosis environment may be related to an increased risk of comorbidly. This study aims to evaluate the nationwide inpatient sample trends and comorbidities associated with endometriosis and compare with fibroids, another high prevalent being gynecologic disease.

**Design:** 10 years cross-section study of Nationwide Inpatients Sample (NIS) between 1998 and 2008.

**Materials and Methods:** We have performed a cross section evaluation of all discharges from NIS database, using a diagnostic identification code for endometriosis and fibroids. A multivariable logistic regression analysis and Poisson regression were performed to determine the odds ratio. Demographics (age,race,income,length of stay) and comorbidities (hypertension;neurological disorders;HIV) were retrieved in both groups.

**Results:** A total of 556,451 patients were identified during the 10 years period of time, including Group A: 81411 patients with endometriosis and Group B: 475040 patients with fibroids. There was no trend regarding number of diagnoses and number of procedures by year. Comparing with fibroids, endometriosis has a significantly reduction risk of any Comorbidity. The odds ratio of having any comorbidity was 0.78 (0.77, 0.79 95%CI; p<0.001). Endometriosis increases significantly the statistical risk of depression and psychoses. (p<0.01) the associations remain significant even after adjusting for race. Fibroids patients had twice and increase odds of having HIV. (0.04vs0.02; p<0.01). There were no different between group A and B in peripheral vascular disorder, renal failure, liver disease and lymphoma.

**Conclusion:** Endometriosis increases the risk of having physiological comorbidities. Our study highlights the importance of follow up psychic and mental health of patients who had a diagnosis of endometriosis. A multidisciplinary team approach is needed.

**Keywords:** Comorbidities endometriosis

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Session - Pathogenesis / aetiology

S3-6

**THE ENDOCANNABINOID SYSTEM MODULATES ENDOMETRIOSIS DEVELOPMENT IN A MOUSE MODEL: INVESTIGATING THE ROLE OF THE CB1 RECEPTOR**

Paola Panina<sup>1</sup>, Ana Maria Sanchez<sup>1</sup>, Paola Vigano<sup>1</sup>, Alessandra Mugione<sup>1</sup>, Guillermo Velasco<sup>2</sup>, Massimo Candiani<sup>1</sup>

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**Objectives:** Cannabinoids have been shown to affect inflammatory response, proliferation and survival, which are critical cellular mechanisms involved in endometriosis. Our goal was study the regulation and function of the endocannabinoid system in a validated mouse model of endometriosis and to verify whether the system might represent a promising therapeutic target.

**Design:** Methanandamide (5mg/kg) was injected i.p. at the time of endometriosis induction in 20 Balb/c female mice, and treatment was repeated 5 d/wk for 2 wks. Endometriosis was also induced in C57Bl/6 CB1<sup>-/-</sup> mice (n=10) and in their wild-type (WT) littermate controls (n=10). Mice were sacrificed 15 days after endometriosis induction.

**Materials and Methods:** Lesions number and size were evaluated. Gene expression of CB1, CB2, NAPE-PLD, FAAH, survivin, N-/E- cadherin, VEGF, TNF $\alpha$ , IL-6, IL-1 $\alpha$ , IL-1 $\beta$ ,  $\beta$ 1integrin were evaluated in eutopic or ectopic endometrium by q-PCR. Levels of IL-6 in the peritoneal fluid was evaluated by specific ELISA.

**Results:** CB1 and CB2 receptors, NAPE-PLD and FAAH were all expressed in eutopic and ectopic tissue. Treatment with methanandamide increased the lesion total volume compared to vehicle-treated mice (p=0.04). Expression of survivin, N-cadherin and  $\beta$ 1-integrin in ectopic endometrium from methanandamide-treated mice were increased compared to vehicle-treated animals. Expression of IL-6 in ectopic endometrium was up-regulated in methanandamide-treated mice compared with vehicle-treated mice (p=0.03). Moreover IL-6 levels were increased in peritoneal fluid of methanandamide-treated mice. Endometriosis was induced in CB1<sup>-/-</sup> mice in order to test the role of the CB1 receptor. Total lesion size was reduced in CB1<sup>-/-</sup> compared to WT mice (p=0.02). Survivin and N-Cadherin were down-regulated in ectopic endometrium of CB1<sup>-/-</sup> mice.

**Conclusion:** These results suggest a role for the endocannabinoid system as a possible mediator of endometriosis development through the up-regulation of pro-survival, adhesion and inflammatory factors. This effect is mediated, at least in part, by the CB1 receptor supporting the possibility to target this pathway for the disease management.

**Keywords:** Cannabinoid, methanandamide

Thursday 1 May 2014

Session - Pathogenesis / aetiology

S3-7

**NERVE FIBER AND LYMPHOID NODULE WERE OBSERVED IN PATHOLOGICAL AND IMMUNOHISTOLOGICAL ANALYSIS OF CYNOMOLGUS MONKEYS (MACACA FASCICULARIS) WITH SPONTANEOUS ENDOMETRIOSIS**

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**Objectives:** This study aims to analyze the histopathology of spontaneous endometriosis in cynomolgus monkeys in detail.

**Design:** Nine cases of spontaneous endometriosis were diagnosed by laparoscopy or necropsy. Their structures (endometrial-like glands, stromal lesions and interstitium outside of stromal lesions) and components (macrophages with yellow pigments, neutrophils, lymph nodes and nerve fiber) were analyzed pathologically and immunohistologically.

**Materials and Methods:** Each endometriosis lesion was dissected from the animal, fixed in 10% neutral buffered formalin, and a paraffin-embedded thin section was HE stained by the conventional method. The tissue sections with appropriate lesions were subjected to immunohistochemistry against  $\alpha$ -smooth muscle actin (SMA), CD10, CD31, and nerve fiber (NF).

**Results:** Pathological observation revealed that each lesion was composed of epithelial elements and stromal/interstitial elements. As for the epithelial elements, endometrial epithelium consisted of glandular lumens, some of which were filled with hemorrhagic red blood cells and neutrophils. In the stromal area located just beneath the endometrial epithelium, spindle-shaped cells similar to those in normal endometrial stromal cells were positive for CD10. In the interstitial area,  $\alpha$ -SMA-positive smooth muscle and azan-positive collagen fibers occupied a large part of the lesion. Within the interstitial area, there were hemorrhage and macrophages with yellow brown pigment, which are typical components reported in endometriosis. Interestingly, lymphoid tissues and NF-positive nerve fibers were observed also within the interstitial area.

**Conclusion:** Typical features seen in human and baboon with spontaneous endometriosis were also observed in cynomolgus monkeys. This is the first report describing the existence in endometriosis in cynomolgus monkeys of nerve fibers that might cause pain and the formation of lymph nodes resulting from chronic inflammation.

**Keywords:** Innervation, fibrosis, lymphoid-tissue

Thursday 1 May 2014

Video Session #1

V1-1

**SURGICAL TREATMENT OF MULTIPLE SITES BOWEL ENDOMETRIOSIS – HOW WE PERFORM**

Luciano Gibran<sup>1</sup>, Patrick Bellelis<sup>1</sup>, Marco Antonio Bassi<sup>1</sup>, Luiz Flávio Cordeiro Fernandes<sup>1</sup>, Sergio Podgaec<sup>1</sup>, Mauricio Simoes Abrao<sup>1</sup>

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**Objectives:** To describe the approach of bowel endometriosis in multiple sites and in different locations in the abdominal cavity.

**Design:** a case report in a 36- year old patient with acyclic pelvic pain, dyspareunia, dyschezia and severe dysmenorrhea. The transvaginal/transabdominal ultrasound with prior bowel preparation identified the presence of bilateral endometriomas, 2 nodules in the ileum, 3 nodules in the rectosigmoid, ileocecal appendix, bilateral uterosacral ligaments and retrocervical region.

**Materials and Methods:** it was performed a videolaparoscopy with adhesiolysis and the identification of the left ureter as the first step. Hereafter, it was executed the preparation of rectum and sigmoid with a margin of at least 2cm for its resection. Than, all other lesions in the abdominal cavity was resected by laparoscopy.

**Results:** The surgery proceeded without any complications and with minimal blood loss. The duration of the procedure was 147 minutes. On day one after surgery it was reintroduced liquid diet. From day two, a light diet , and the progression according to the patient's response. The patient had minimal pain (VAS 3) on the postoperative and with preservation of bowel and vesical function. Received discharge in the 4th day after surgery.

**Conclusion:** Multiple intestinal lesions require surgical treatment by segmental resection and not the performance of multiple discoid resections because it should increased chance of leakage and stenosis.

**Keywords:** Endometriosis, bowel, treatment

Thursday 1 May 2014

Video Session #1

V1-2

**LAPAROSCOPIC E/O ULTRALOW RECTAL ,BLADDER,PELVIC ENDOMETRIOSIS**

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**Objectives:** Laparoscopic excision of severe endometriosis

**Design:** Pouch of Douglas - obliterated, rectum puckered towards right uterosacral ligament Uterovesical space - multiple deep endometriotic implants up to 2 cm

**Materials and Methods:** Bladder - full thickness 3x3x3 cm endometriotic nodule at bladder dome, left of midline, clear of ureteric orifices

**Results:** Rectovaginal septum - huge 5x5x4cm endometriotic nodule infiltrates into posterior fornix, uterosacral junction, right para-rectal sidewall, right uterosacral ligament, under right uterine vessels, firmly onto right levator ani fascia Dissection to isolate rectovaginal nodule off posterior cervix, left and right uterosacral ligaments, into and off posterior vagina, lesion isolated onto anterior rectum. Posterior colpotomy repaired with 0-Vicryl sutures. Further dissection to free rectal nodule off levator fascia, followed by total mesenteric rectal resection Rectal nodule removed by segmental resection, delivered via minilaparotomy incision, followed by ultra-low rectal reanastomosis with endoscopic stapling device Rectal insufflation with air using bulb syringe per anus, clamping of rectosigmoid with soft bowel clamps, to carefully assess for any rectal wall defect / leakage

**Conclusion:** Laparoscopic e/o ultralow rectal, bladder, pelvic endometriosis, reanastomosis

**Keywords:** Laparoscopic e/o endometriosis

Thursday 1 May 2014

Video Session #1

V1-3

**RESECTION OF ENDOMETRIOSIS OF THE LEFT LATERAL INFRA URETERIC AND SUPRA URETERIC PARAMETRIUM**

Jennifer Uzan<sup>1</sup>, Cyrille Huchon<sup>2</sup>, Arnaud Fauconnier<sup>2</sup>

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**Objectives:** Explain the surgical technique for the resection of endometriosis of the lateral infra and supra ureteric parametrium

**Design:** Laparoscopy assisted surgery. Exploration of the pelvis and surgical treatment of deep infiltrating endometriosis (DIE) of the parametrium.

**Materials and Methods:** Endometriosis of the vesicouterine space, with infiltration of the anterior uterine serosa, the left round ligament and transfixion of the left broad ligament backwards to the left ovarian dimple through the supra ureteric and infra ureteric parametrium. Infiltration of the left ureter adventice and the left uterine artery.

**Results:** Intra fascial dissection of the anterior uterine serosa permitted to reveal the lateral extension to the left broad ligament through the parametrium. Left ureterolysis was proceeding until the crossing with uterine artery, which was infiltrated by the DIE and then sacrificed. We followed up left ureterolysis in the left supra ureteric parametrium, which permitted to liberate the ureter and the left horn bladder adherent to the DIE. DIE was infiltrating the left uterosacral ligament and the ascending part of the left uterine artery. Then, the dissection ended with the section of the ascending part of the uterine artery and the extra fascial dissection of the left uterosacral ligament to liberate the DIE.

**Conclusion:** Progressive dissection permitted to proceed to a radical but conservative treatment of the DIE.

**Keywords:** Endometriosis

Thursday 1 May 2014

Video Session #1

V1-4

**ROBOTIC ADENOMYOMECTOMY TO PRESERVE THE UTERUS FOR FUTURE PREGNANCY**

Sang Hoon Kwon<sup>1</sup>, Soon Do Cha<sup>1</sup>, Chi Heum Cho<sup>1</sup>, Seok Ju Seong<sup>2</sup>

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**Objectives:** This video introduce Robotic treatment for adenomyosis especially focal adenomyoma

**Design:** We underwent robotic adenomyomectomy to save uterus

**Materials and Methods:** We inject vassopressin on uterine body and uterine artery ligation to control bleeding. We make vertical incision of anterior wall of uterus by cautery spatula. We resected easily adenomyoma tissue via bidirectional traction. We suture two serosal layer of uterine body by overlap. We removed resected tissue by morcellator

**Results:** Robotic adenomyomectomy provide three-dimensional views, degree of freedom of movement, less surgeon fatigue. There also are several merits that It is superior visualization, complete control of resection angle, self assist on delicate resection, improved multiple layer suturing. We easily perform to excision of focal adenomyosis by da Vinci robotic surgery. So it could be safe and effective surgical method.

**Conclusion:** This video focus on the great dexterity allowed by articulation of instruments which allow meticulous dissection and overlap reconstruction of uterine layers

**Keywords:** Robot, adenomyomectomy

Thursday 1 May 2014

Video Session #1

V1-5

**BOWEL ENDOMETRIOSIS - ROBOTIC TREATMENT WITH DISCOID RESECTION - THE TECHNIQUE**

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**Objectives:** The purpose of this video is to present a technique of a robotic discoid resection of endometriotic nodule in the bowel.

**Design:** Serial cases results.

**Materials and Methods:** 10 patients underwent to discoid resection with this robotic technique using da Vinci system. All procedures were performed in the same hospital of high complexity, located in São Paulo - Brazil.

**Results:** Ten patients underwent for intestinal discoid resection of endometriotic nodule by robotic technique. One of them, presented mucosa bleeding in posterior wall, due to incorrect technique. The bleeding was self-limited, evaluated by colonoscopy. All cases have evolved without stenosis or any other complications related to the procedure in 36 months of follow-up.

**Conclusion:** The technique has a low morbidity, high resolution and is easily reproducible. The great advantage is to be minimally invasive with complete preservation of pelvic innervation. The risks of complications diminishes as we observe all technical standards.

**Keywords:** Colectomy; Robotic; Endometriosis;

Thursday 1 May 2014

Video Session #1

V1-6

**ADVANTAGE TECHNICAL ASSOCIATE OF SHAVE SURGERY IN THE ENDOMETRIOSIS  
INFILTRATING SEGMENTAL RESECTION**

Univaldo Sagae<sup>1</sup>, Doryane Lima<sup>2</sup>, Gustavo Kurachi<sup>3</sup>, Namir Cavalli<sup>4</sup>, Helin Minoru Matsumoto<sup>5</sup>, Lucia Sagae<sup>5</sup>

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**Objectives:** Demonstrate technical alternatives for parts surgical extraction via anal in patients with intestinal segment and deep endometriosis.

**Design:** Prospective study involved 20 women undergoing surgical management of deep infiltrating endometriosis from August 2012 to August 2013, whose colorectal involvement had been assessed by magnetic resonance imaging and rectal tridimensional ultrasonography (3D-US). Patients with intestinal involvement on 3D US were treated with multidisciplinary videolaparoscopic surgery.

**Materials and Methods:** Twenty patients were included in the study with 3D-US findings with small lesions extended as far as the perirectal fat or lesions the rectal layers. Then, they underwent to diathermy excision with shave excision and after putting the foci endometriosis into circular stapler to segmental low anterior resection by endoanal.

**Results:** The mean age was 32.4 years. The mean estimated diameter of the nodule felt by 3D-US was 1.8 cm. Laparoscopic surgery was performed by a team of gynecologists and colorectal surgeons in all patients and the mean operative time was 155 minutes. We didn't have intraoperative and postoperative complications. Shaving presented without complications and feasible.

**Conclusion:** Surgery for deep endometriosis is feasible and this technique decrease operation time, no increase morbidity and it doesn't necessary abdominal incision.

**Keywords:** Endometriosis infiltrating; resection

**Thursday 1 May 2014**

**Video Session #1**

**V1-7**

**THERE IS MORE TO ENDOMETRIOSIS THAN WE CAN SEE**

Tamer Seckin<sup>1</sup>

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*No Abstract Available*

Friday 2 May 2014

Seminar #5 - Pain and pain mechanisms

M5-1

**ESTROGEN RECEPTOR SUBTYPE DEPENDENT MACROPHAGE ACTIVATION LEADS TO A SENSORY NERVE OUTGROWTH IN PERITONEAL ENDOMETRIOSIS**

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**Objectives:** Endometriosis has some similarities with inflammatory autoimmune diseases. It exhibits a dominance of proinflammatory peptidergic nerve fibers (NF) over noradrenergic anti-inflammatory NF, altered cytokine levels and an increased incidence of macrophages. The interaction of immune cells, estrogen (E2) and NF may modulate inflammation and pain mechanisms in endometriosis.

**Design:** E2 not only influences pain perception, but mediates the innate and adaptive immune system, by influencing cytokine production and activation of immune cells. In order to evaluate, how estrogen receptor (ER) subtype specific signalling regulates neuro-modulatory effects of macrophages during peritoneal endometriosis, ex vivo and in vitro analysis were performed.

**Materials and Methods:** Human M1, M2 macrophages and rat dorsal-root-ganglia-neurons (DRGs) were treated with E2, DPN (ER $\beta$ -agonist) or PPT (ER $\alpha$ -agonist) with or without an ER antagonist (ICI12780). Expression of ERs, neurotrophins/neurotrophin receptors and IL-1 $\beta$ /IL-1R2 was determined by qPCR and/or Western blotting. DRGs were treated with macrophage-conditioned media (CM) to evaluate neurite outgrowth

**Results:** ERs were present in human M1, M2 macrophages and rat DRGs. CM from M1 and M2 macrophages treated with E2 significantly enhanced neurite outgrowth from DRGs compared to CM from controls, this was abrogated by an ER antagonist. The expression of neurotrophic factors was significantly up-regulated by E2 in M2 but not in M1 macrophages, expression of neurotrophin receptors was increased in DRGs incubated with E2. TrkB, the receptor for BDNF was significantly up-regulated by all treatments (including ICI12780). TrkC, (high affinity NT-3 receptor) was significantly up-regulated by E2, via ER $\alpha$  and ER $\beta$ . IL-1 $\beta$  was significantly upregulated in both DRGs and M2 macrophages in the presence of E2, but the scavenger IL-1R2 was highly upregulated via ER $\beta$ , demonstrating the anti-inflammatory effect of ER $\beta$

**Conclusion:** This study reveals how E2 modulates the macrophage-NF crosstalk in endometriosis. E2 activates a macrophage phenotype, which secretes neurotrophins and pain-mediators and increases the sensitivity of DRGs towards neurotrophins. This crosstalk seems to facilitate the chronic and painful condition of endometriosis, but it might be modulated via ER subtype-selective antagonists.

**Keywords:** Estrogen, macrophages, neurotrophins

Friday 2 May 2014

Seminar #5 - Pain and pain mechanisms

M5-2

**INHIBITION OF PGE2 RECEPTORS EP2 AND EP4 DECREASES GROWTH, INNERVATION, AND NOCICEPTION OF ENDOMETRIOSIS**

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**Objectives:** Prostaglandin E2 (PGE2) produced at the site of inflammation acts on the nociceptors of peripheral terminals through EP1, EP2, EP3, and EP4 receptors. Our working hypothesis is that pharmacological systemic blockade of EP2 and EP4 inhibits growth and innervations and nociceptive mechanisms of endometriosis.

**Design:** Mixed population of human endometriotic epithelial cells (12Z-GFP) and stromal cells (22B-RFP) were xenografted (day 0) into the peritoneal cavity of six-week old Rag2<sup>fl/c</sup> ovariectomized mice supplemented with estrogen. On day 15, Group-1 (n=6) mice were served as control and Group-2 (n=6) mice were treated with EP2 and EP4 inhibitors.

**Materials and Methods:** On day 30, nociception and pain sensitivity of the experimental mice was examined using pain behavior models, growth of endometriosis was measured using bioimager and fluorescence microscopy, and then peritoneal endometriosis lesions were collected.

**Results:** A linear increase of 12Z-GFP or 22B-RFP cells was detected with the in vivo imager. Using a fluorescence stereo microscope, ~18-20 lesions were detectable in the peritoneal cavity. Selective inhibition of EP2 and EP4: (i) decreased growth of endometriosis up to 50-60%; (ii) decreased expression of neural markers protein gene product 9.5 (PGP 9.5), substance P (SP), calcitonin gene-related peptide (CGRP) and vesicular monoamine transporter (VMAT), and vanilloid receptor TRPV1 in innervations of endometriosis; (iii) decreased nociception and pain sensitivity in experimental endometriosis mice.

**Conclusion:** These results together indicate that selective inhibition of EP2 and EP4 decreases growth, innervations, and nociception of endometriosis in humanized endometriosis mice models.

**Keywords:** PGE2, pain, Endometriosis

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Seminar #5 - Pain and pain mechanisms

M5-3

**NOVEL MECHANISMS OF NOCICEPTION IN ANIMAL AND CELL MODELS OF ENDOMETRIOSIS**

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**Objectives:** One of the most debilitating symptoms associated with endometriosis is chronic pain. Our laboratory aims to better understand the mechanisms leading to pain in women with endometriosis. The goal of this study was to assess whether lipoproteins present in the peritoneal fluid (PF) induce nociception in endometriosis.

**Design:** We used in vivo and in vitro models of endometriosis to investigate the impact of PF-derived lipoproteins on nociceptive activity. Peritoneal fluid from patients with +endometriosis/+pain, +endometriosis/-pain, and -endometriosis/-pain or lipoproteins with varying levels of oxidation were used to test their nociceptive activity.

**Materials and Methods:** Animals were injected with lipoproteins of varying oxidation or PF from patients and assessed for nociception using the Hargreaves assay of paw-withdrawal latency. Ishikawa endometrial cells were also treated with similar conditions and changes in the expression of nociceptive genes using the Pain: Neuropathic and Inflammatory PCR array were determined.

**Results:** In in-vivo studies, the lipoproteins that had undergone oxidation (similar to that present in the PF of women with endometriosis) had the ability to induce nociception as seen by shorter paw-withdrawal latency ( $p < 0.05$ ). This pain response was effectively prevented by antioxidants than with non-steroidal anti-inflammatory drugs (NSAIDs). In in-vitro studies using Ishikawa cells, several nociceptive and inflammatory genes were upregulated when treated with lipoproteins compared to untreated controls. Inflammatory and nociceptive genes such as interleukin-2 and 6, opioid receptors and genes that belong to the voltage-gated sodium channels (SCN10A, 11A, 3A and 9A) were upregulated by both lipoproteins and PF from patients with pain compared to controls.

**Conclusion:** PF-derived lipoproteins are capable of eliciting a nociceptive response in both animal (which is alleviated by antioxidants) and cell models of endometriosis. More studies are needed to identify the target genes responsible for this novel mechanism of nociception and future therapy for pain in endometriosis.

**Keywords:** Endometriosis, nociception, oxidation

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Seminar #5 - Pain and pain mechanisms

M5-4

**ESTROGEN RECEPTOR SUBTYPES MODULATE HOW NERVE FIBRES INFLUENCE BLOOD VESSELS AND MACROPHAGES IN PERITONEAL ENDOMETRIOSIS**

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**Objectives:** Endometriosis lesions exist in an estrogen dominated microenvironment. Nerves, vessels and macrophages are closely associated in lesions. Neurons innervating the uterus and peritoneum are ER $\alpha$ +/ER $\beta$ +. Our objective is to understand how estrogens and their receptors (ER $\alpha$  and ER $\beta$ ) regulate the cellular interplay between nerves, vessels and macrophages in peritoneal endometriosis.

**Design:** Recruitment of vessels and nerves (neuroangiogenesis) was investigated in lesions established de novo in a mouse model and in human samples. Regulatory molecules responsible for the interplay between nerves, vessels and macrophages and the role of estrogens (E) and ERs was investigated.

**Materials and Methods:** Endometrium, peritoneum, endometriosis lesions from women with/without endometriosis and samples from a mouse model of endometriosis were obtained. Rat dorsal root ganglia neurons (DRGs), human endometrial endothelial cells (HEECs) and human peripheral blood monocyte derived macrophages (PBDMs) were used in functional assays. Expression of ERs and regulatory factors was quantified.

**Results:** Endothelial cells lining the vessels of endometriosis lesions are ER $\beta$ +/ER $\alpha$ - but the tissue resident macrophages are ER $\alpha$ +/ER $\beta$ +. In vitro, DRGs, HEECs and PBDMs had identical ER profiles to in vivo equivalents. Expression of the axonal guidance factor Slit3 was significantly increased in lesions (P=0.001) and E-regulated in DRGs. Conditioned media (CM) from DRGs treated with the ER $\alpha$  agonist PPT significantly increased network formation (angiogenesis assay; P=0.05) in HEECs. This paracrine effect was abrogated using an anti-Slit3 antibody. We also documented ER dependent changes in expression of macrophage stimulating factors (M-CSF/GM-CSF), chemokines (CCL2 / CCL3) and substance P in DRGs; macrophages migrated towards DRG conditioned media. Once recruited to nerve fibres M2 polarised macrophages exhibited ER-dependent neurotrophic properties.

**Conclusion:** We have documented evidence supporting a key role for ER-dependent regulation of the interplay between nerves, vessels and macrophages. Our studies offer important insights into how neuroangiogenesis and neuro-immune interactions in endometriosis may be modulated and can inform development of new therapies.

**Keywords:** Endometriosis, macrophage, neuroangiogenesis.

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Seminar #5 - Pain and pain mechanisms

M5-5

**DO CLINICAL PAIN MEASURES CORRELATE TO SUBCORTICAL BRAIN VOLUME IN WOMEN WITH CHRONIC PELVIC PAIN?**

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**Objectives:** Chronic pelvic pain (CPP) affects up to 40% of women worldwide and has previously been associated with alterations in brain volume. Other markers of central change in CPP have been related to specific disease measures/characteristics. We aim to investigate whether brain volume in these women is influenced by such measures.

**Design:** A prospective cohort study using structural and functional magnetic resonance imaging (fMRI) of the brain.

**Materials and Methods:** 14 women (recruited from Edinburgh and Oxford) with CPP rated their pain severity (using a numeric pain score (NRS)), estimated their pain duration and underwent an MRI brain (Siemens 3T). Structural data were analysed using FIRST "FAST" from FMRIB's software library (FSL). Statistical analysis was performed with SPSS (version 19).

**Results:** Baseline descriptive statistics demonstrated comparability between the Oxford and Edinburgh cohorts. The median pain score was 4 (range 1.5-5.5). Bivariate correlation analyses between pain scores and subcortical volumes showed no significant correlation (overall brain volume ( $p=0.362$ ) as well as thalamic (left/right:  $p=0.564/p=0.623$ ), hippocampal (left/right:  $p=0.915/p=0.976$ ) and amygdalic (left/right:  $p=0.401/p=0.939$ ) volumes). Similarly, there were no significant correlations between duration of pain and brain volume. Partial correlation to determine the relationship between the subcortical volumes and pain scores while controlling for age also again showed no significant correlation. Total grey matter volume was also not correlated to pain scores ( $p=0.334$ ) or duration ( $p=0.888$ ) either overall or partially when controlling for age (pain:  $p=0.359$ ; duration:  $p=0.888$ ).

**Conclusion:** Our data suggest that in women with CPP brain volume is not related to severity or duration of pain. This may be due to the heterogeneity of pain symptoms experienced by these women (dysmenorrhoea, dyspareunia, non-cyclical pain) but could also reflect other factors such as analgesic use and endocrine status.

**Keywords:** MRI, brain, pain

Friday 2 May 2014

Seminar #6 - New drugs

M6-1

**FIRST PEPTIDE-BASED NON-HORMONAL THERAPY OF ENDOMETRIOSIS: WHERE ARE WE TODAY?**

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**Objectives:** Synuclein-gamma (SNCG), an established causative of cell proliferation and metastasis has elevated expression in endothelial cells of endometriosis lesions compared to eutopic endometrium. Objectives were to evaluate the efficacy of a SNCG targeting peptide in vitro and in human endometriotic lesion development in vivo using a xenograft mouse model.

**Design:** We propose that blocking SNCG function with a peptide inhibitor will prevent the neovascularization and growth of human endometriotic lesions in a xenograft mouse model.

**Materials and Methods:** The SNCG-targeting peptide, SP012, is a 10 amino acid peptide attached to cell penetrating TAT sequence. Specific in vitro interaction assays, cell proliferation assays, confocal and intra vital microscopy and flow cytometry was used to assess mechanistic properties of SNCG in proliferation of endometriosis and inhibition via SNCG targeting peptide.

**Results:** Co-immunoprecipitation and a battery of biophysical experiments demonstrated that SP012 specifically binds to SNCG. SP012 reduced human umbilical vein endothelial cell (HUVEC) and EECC proliferation in vitro. Human endometriotic lesions, surgically engrafted into the peritoneal cavity of female alymphoid Rag2(-/-)Il2rg(-/-) mice, had reduced blood vessel growth when given daily intraperitoneal injections of SP012 compared to phosphate buffered saline control. Preliminary CD31 immunofluorescence of human endometriotic lesions revealed that microvessel density was lower in SP012-treated lesions compared to control. In a separate experiment, SP012-FITC injected into the peritoneal cavity of alymphoid female mice surgically induced with human endometriotic lesions was uptaken by cell types in endometriotic lesions when visualized using intravital confocal microscopy.

**Conclusion:** These in vitro and in vivo studies indicate that the targeted inhibition of SNCG can affect the neovascular development of endometriosis lesions. Further characterization of drug-like properties of the peptide suggests that it has promise to be a potential therapeutic option for the treatment of endometriosis in future

**Keywords:** Non-hormonal, peptide-drug, xenograft

Friday 2 May 2014

Seminar #6 - New drugs

M6-2

**PHARMACOKINETICS OF ELAGOLIX, AN ORAL GONADOTROPIN-RELEASING HORMONE (GNRH) ANTAGONIST TARGETED IN THE TREATMENT OF ENDOMETRIOSIS AND UTERINE LEIOMYOMAS**

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**Objectives:** To assess pharmacokinetics and safety of single and multiple doses of elagolix in healthy premenopausal females enrolled in two Phase 1 studies.

**Design:** 45 healthy adult premenopausal females were randomized to receive elagolix 150 mg once daily (QD), 100 mg, 200 mg, 300 mg, 400 mg twice daily (BID), or placebo for 21 days. Another 18 healthy adult females were randomized to receive single doses of elagolix 600 mg, 900 mg or placebo.

**Materials and Methods:** Single and multiple-dose intensive pharmacokinetic blood samples for elagolix assay were collected. Pharmacokinetic analyses were conducted using Pharsight Phoenix WinNonlin and statistical analyses were performed using SAS. Safety for both studies was evaluated through adverse event (AE) monitoring, vital signs, physical examination, ECG, and laboratory tests assessments.

**Results:** Elagolix has a linear pharmacokinetic profile, with dose proportional, steady-state maximum concentrations (C<sub>max</sub>) and area-under-the-curves (AUCs) up to 400 mg BID. For the 600 mg and 900 mg single doses, a more than dose proportional increase in elagolix concentrations was observed. Elagolix was generally well tolerated up to 400 mg BID and 900 mg single dose. In the multiple dose study, 27/34 (79%) subjects receiving elagolix and 10/11 (91%) receiving placebo reported at least one treatment emergent AE. Headache, hot flush, abdominal pain, diarrhea and dizziness were the most frequently reported AEs. The majority of AEs were assessed by the investigator as mild in severity. No clinically significant vital signs, ECG or changes in laboratory values were observed during the course of the studies.

**Conclusion:** Elagolix shows a dose proportional increase in exposure in healthy premenopausal adult women, which provides a pharmacokinetic basis for dose-dependent suppression of the pituitary-gonadal axis in women with endometriosis and uterine leiomyomas. Elagolix had an acceptable safety and tolerability profile at doses up to 400 mg BID for 21 days.

**Keywords:** Elagolix, GnRH, antagonist

Friday 2 May 2014

Seminar #6 - New drugs

M6-3

**TARGETING Y-BOX-BINDING PROTEIN 1 (YB-1) FOR THE TREATMENT OF ENDOMETRIOSIS**

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**Objectives:** We recently showed the role of YB-1 in endometriotic epithelial cell expansion and survival. Thus, we prompted to test the therapeutic effect of OSU-03012, a novel and potent celecoxib-derivative, on impairing endometriosis progression in in vitro and in vivo models based on its ability to indirectly block YB-1 function.

**Design:** Z12-cells were exposed to OSU-03012 for 24, 48 or 72 h. Endometriosis was induced in sexually mature C57BL/6J mice (n=25) by autologous transplantation. Transplantation was confirmed 20-days post-surgery by in vivo magnetic resonance imaging (MRI). Oral treatment with OSU-03012 (100 mg/kg) or vehicle-solution (DMSO) were daily ministered for 2-weeks.

**Materials and Methods:** The effect of OSU-03012 on Z12 cell proliferation was assessed by MTT (3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyl-tetrazolium bromide) assay. Upon treatment completion, the autologously transplanted mice were sacrificed and endometrial implants were excised, measured and fixed. Immunohistochemistry for proliferating cell nuclear antigen (PCNA) was performed to assess cell proliferation in the induced endometriotic lesions.

**Results:** OSU-03012 was cytotoxic to Z12 cells in a dose-dependent manner. The concentration of OSU-03012 that was lethal to 50% of cells (LC<sub>50</sub>) after 24 and 48 h of exposure to the drug was 8 and 7 µM, respectively. The respective LC<sub>50</sub> for Z12 cells was slightly lower at 72 h. Endometriotic lesion size was significantly reduced in OSU-03012-treated mice (27.57 ± 3.97 mm<sup>3</sup>) compared to those from the control group (50.50 ± 6.92 mm<sup>3</sup>, P<0.0001). The pre- and post-treatment MRI measurements of the grafts volume revealed that OSU-0312 therapy substantially reduced the endometrial implant size about ~40%. Accordingly, a reduction of 36.6% of the proliferative endometrial cells was detected in induced endometriotic lesions exposed to OSU-03012 treatment.

**Conclusion:** Targeting YB-1 via OSU-03012 showed a potent anti-proliferative effect on in vitro and in vivo endometriosis models and supported the regression of experimental peritoneal endometriosis. These preliminary data suggest that OSU-03012 might be helpful for the treatment of endometriosis and provide a rationale for further testing in in vivo models.

**Keywords:** Endometriosis, YB-1, OSU-03012

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Seminar #6 - New drugs

M6-4

**INHIBITION OF TYPE 1 17 $\beta$ -HYDROXYSTEROID-DEHYDROGENASE IMPAIRS THE SYNTHESIS OF ESTROGENS IN ENDOMETRIOSIS**

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**Objectives:** Endometriosis is estrogen-dependent. The endometriosis tissue can produce estrogens in an autocrine/paracrine manner. This is due to the high activity of the 17 $\beta$ -hydroxysteroid-dehydrogenases (17 $\beta$ -HSDs), enzymes that generate estrogens from inactive precursors. **OBJECTIVE:** Identify the 17 $\beta$ -HSD(s) generating estrogens in endometriosis and test the possibility to inhibit these enzymes for therapeutic purposes.

**Design:** The expression of different 17 $\beta$ -HSDs involved in the estrogen synthesis was assessed in eutopic and ectopic tissue. These biopsies had confirmed unbalanced local 17 $\beta$ -HSD activity, which caused high estrogen generation in endometriosis. The possibility to block the synthesis of estrogens by one inhibitor specific for 17 $\beta$ -HSD-1 was assessed.

**Materials and Methods:** Expression of the 17 $\beta$ -HSDs was measured by real time PCR. Eutopic and ectopic tissue from endometriosis patients (n=14) was used. The effect of the inhibitor specific for 17 $\beta$ -HSD-1 was assessed by high-performance-liquid-chromatography (HPLC) in tissue lysates from endometriosis tissues (n=27).

**Results:** In all but one patient, high 17 $\beta$ -HSD-1 level was associated with the increased estrogen synthesis in endometriosis. Inhibition of 17 $\beta$ -HSD-1 restores to various extents, depending on the patient, the correct metabolism. In 19 out of 27 patients analysed (70%) the 17 $\beta$ -HSD-1 inhibitor decreased the generation of estrogens by over 85%.

**Conclusion:** Inhibition of 17 $\beta$ -HSD-1 can be a potential future treatment option aimed at restoring the correct metabolic balance of estrogens in endometriosis patients with increased local 17 $\beta$ -HSD-1 enzyme activity.

**Keywords:** 17 $\beta$ -hydroxysteroid-dehydrogenase-type-1; estrogens; endometriosis

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Seminar #6 - New drugs

M6-5

**DUAL-PROGESTOGEN-DELIVERY SYSTEMS THERAPY WITH LEVONORGESTREL INTRAUTERINE SYSTEM AND ETONOGESTREL SUBDERMAL IMPLANT FOR REFRACTORY ENDOMETRIOSIS-ASSOCIATED PELVIC PAIN: AN EFFECTIVE NEW THERAPY.**

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**Objectives:** To determine if the simultaneous use of dual progestogen-delivery systems (DPS) with the levonorgestrel intrauterine system (LNG-IUS) and etonogestrel subdermal implant (ESI) be an effective new therapy for refractory endometriosis-associated pelvic pain.

**Design:** This report details the very successful simultaneous use of a levonorgestrel-releasing intrauterine system (LNG-IUS) combined with an etonogestrel subdermal implant (ESI) for debilitating and refractory endometriosis in 40 women. The duration of therapy ranged from 9 – 98 months.

**Materials and Methods:** Medical records (n=40) of two clinicians who utilised the DPS were searched. These 40 patients' used the DPS following failure of various first-line and/or advanced medical therapies. Mean duration of symptoms (dysmenorrhoea, deep dyspareunia, dyschezia, heavy menstrual bleeding and other symptoms) was 7.9 (range 0.5–30) years.

**Results:** Overall, responses were particularly favourable in a difficult group of adolescents (n=4; 10%) who had "dramatic" improvement (amenorrhoea with no pelvic pain). Marked improvement (major resolution of symptoms) was reported in 26/40 (65%). Three had borderline initial response, then obtained marked ongoing improvement (with short-term additional therapy), 5 reported borderline benefit and 7 women had either the LNG-IUS or ESI or both systems removed due to some persistent pain or side-effects.

**Conclusion:** The DPS is an effective new treatment option in women with persistent endometriosis-associated symptoms who have failed multiple advanced medical therapies and/or conservative surgery. A randomised controlled trial comparing the dual therapy versus LNG-IUS alone is warranted to determine broader application of this novel therapy in management of endometriosis symptoms.

**Keywords:** Endometriosis, progestogens, pain

Friday 2 May 2014

Seminar #7 - Non-invasive diagnosis

M7-1

**ULTRASOUND MAPPING OF PELVIC ENDOMETRIOSIS: DOES THE LOCATION AND NUMBER OF LESIONS AFFECT THE DIAGNOSTIC ACCURACY? A MULTICENTRE DIAGNOSTIC ACCURACY STUDY.**

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**Objectives:** To assess the accuracy of pre-operative transvaginal ultrasound scanning (TVS) in identifying the specific features of pelvic endometriosis (including deeply infiltrating endometriosis (DIE) and pelvic adhesions especially ovarian) in comparison with laparoscopy. Also to assess the effect that the number of lesions has on the diagnostic accuracy.

**Design:** This was a prospective, observational, multicentre diagnostic accuracy study. Women with suspected endometriosis had a TVS performed preoperatively and the findings compared with the subsequent laparoscopy. The ultrasound operators were blinded to any previous surgical findings. The operating surgeons were blinded to the detailed transvaginal ultrasound findings.

**Materials and Methods:** Consecutive women with clinically suspected or proven pelvic endometriosis, who were booked for laparoscopy, were invited to join the study. They all underwent a systematic transvaginal ultrasound examination in order to identify discrete endometriotic lesions and pelvic adhesions. The findings were recorded using the revised ASRM endometriosis severity classification.

**Results:** 198 women who underwent preoperative TVS and laparoscopy were included in the final analysis. At laparoscopy 126/198(63.6%) women had evidence of pelvic endometriosis. 28/126(22.8%) had endometriosis in a single location whilst the remaining 98/126(77.2%) had endometriosis in two or more locations. Positive likelihood ratios (LR+) were >10 for the ultrasound diagnosis of ovarian endometriomas, moderate or severe ovarian adhesions, pouch-of-Douglas adhesions, and DIE of bladder, recto-sigmoid colon, rectovaginal area, uterovesical-fold and uterosacral-ligament. The negative likelihood ratio (LR-) was: <0.1 for bladder DIE; 0.1-0.2 for ovarian endometriomas, moderate or severe ovarian adhesions, and pouch-of-Douglas adhesions; 0.5-1 for rectovaginal, uterovesical-fold, pelvic-side-wall and uterosacral-ligament DIE. The accuracy of TVS for both total number of endometriotic lesions and DIE lesions significantly improves with increasing total number of lesions.

**Conclusion:** Our study shows that the TVS diagnosis of endometriotic lesions is specific with rare false positives. The assessment of ovarian adhesions is accurate which has not been shown before. Negative findings are less reliable. The accuracy of ultrasound diagnosis is significantly affected by the location and number of endometriotic lesions.

**Keywords:** Diagnosis, severity, adhesions

Friday 2 May 2014

Seminar #7 - Non-invasive diagnosis

M7-2

**EVALUATION OF AN INNOVATIVE MODEL OF CARE AND DEDICATED SERVICE FOR TEENAGERS AND WOMEN WITH PERIOD PAIN, PELVIC PAIN AND ENDOMETRIOSIS**

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**Objectives:** To examine outcomes and patient satisfaction for an innovative multidisciplinary healthcare model for women with period pain, pelvic pain and endometriosis that empowers with knowledge, self-management skills and ownership/responsibility. Current medical models disempower women and create an expectation to be 'fixed' with pills or surgery with little self-responsibility for outcomes.

**Design:** Qualitative and quantitative data from three studies: 1. Focus group research on the impact of endometriosis (N=35); 2. Evaluation of nurse-led education of teenagers and women with period pain, pelvic pain and endometriosis (N=15); 3. Diagnosis and screening accuracy of a dedicated endometriosis service, assessed by negative laparoscopy rate.

**Materials and Methods:** At initial visit a nurse-led comprehensive history identifies all health issues. Issues are prioritised and a care plan devised for further consultation with medical and allied health professionals as required. General health information includes lifestyle and other support measures. Subsequent visits monitor progress until symptom management is achieved +/- surgery.

**Results:** Focus group research identified clear differences between standard practice and a dedicated service. Differences related to: time for clients to discuss health and have questions answered; information provided; breadth of options; and self-management skills. Evaluation of nurse-led education was effective where women reported increases in knowledge, a change in thinking and new actions to manage health. Assessment tools used by the dedicated service accurately diagnosed endometriosis or other causes of pelvic pain with a negative laparoscopy rate of <5%.

**Conclusion:** A dedicated multidisciplinary endometriosis and pelvic pain service results in improved patient satisfaction, knowledge and self-management of symptoms and more accurate diagnosis. Future research should examine long term sustainability and outcomes of this model of care.

**Keywords:** Endometriosis, empowerment, self-management

Friday 2 May 2014

Seminar #7 - Non-invasive diagnosis

M7-3

**SCREENING TOOL FOR EARLY-STAGE ENDOMETRIOSIS IN PATIENTS WITH CHRONIC PELVIC PAIN**

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**Objectives:** To develop a non-invasive screening tool for patients with chronic pelvic pain, to discriminate between patients with and without early-stage endometriosis. The goal is have a screening tool with a high sensitivity and reasonable specificity.

**Design:** Prospective, non-randomized, controlled study (Canadian Task Force classification, II-2). Women of reproductive age with chronic pelvic pain (for more than 6 months despite medical therapy, January 2012-June 2013), seen at the Saint Louis University Center for Endometriosis, and found to have early-stage endometriosis or not based on histology.

**Materials and Methods:** Typical pain symptoms and other screening questions pertinent to the effect on activities of daily life were asked preoperatively. Individual categorical variables were tested using chi-squared tests, and continuous variables by the Mann-Whitney U test. In addition, new binary variables were created to test specific combinations of answers.

**Results:** 90 patients found to have early stage disease completed preoperative surveys. Of these, 70 (77.8%) had histologically-confirmed endometriosis and 20 (22.2%) were confirmed not. Variable combinations made it possible to create a predictive model for early-stage endometriosis with excellent discriminatory ability (area-under-the-curve of 0.822,  $p < 0.001$ ). This model was generated using a multi-staged, backwards stepping logistic regression analysis with all variables that were uni-variately significant included in the initial model ( $p < 0.025$ ). The final model had 80.5% sensitivity and 57.7% specificity. This meets the proposed guidelines for useful screening tools of maximal sensitivity (>80%) and acceptable specificity (>50%). The model also allows for an individual probability of dis-ease to be calculated for each patient.

**Conclusion:** A clinically useful, symptom-based screening tool was developed for early-stage endometriosis in patients with chronic pelvic pain seen at a tertiary referral center. The preliminary model has a very high discriminatory ability and can produce an individualized chance of disease. Further large, multi-center validation studies are needed.

**Keywords:** Endometriosis, diagnosis, screening

Friday 2 May 2014

Seminar #7 - Non-invasive diagnosis

M7-4

**A COMBINED APPROACH OF NERVE FIBER DETECTION PLUS INFRARED SPECTROSCOPY PROFILE IN EUTOPIC ENDOMETRIUM OUTPERFORMS THE CAPACITY OF EACH SINGLE TECHNIQUE TO NON-INVASIVELY DIAGNOSE ENDOMETRIOSIS**

Raul Gomez<sup>1</sup>, Hortensia Ferrero<sup>1</sup>, Frank Martin<sup>2</sup>, David Guaita<sup>3</sup>, Carlos Simon<sup>4</sup>, Antonio Pellicer<sup>5</sup>

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**Objectives:** To evaluate the sensitivity and specificity in the diagnosis of endometriosis provided by combining the immunohistochemical detection of nerve fiber and the infrared spectral profile of eutopic endometrial biopsies

**Design:** Endometrial biopsies (N=72) were taken from healthy (N=38) and (grade I-IV) endometriosis (N=34) affected patients during laparoscopic surgery. Samples were fixed in paraformaldehyde and subsequently dehydrated for subsequent immunohistochemical detection of PGP 9.5 (nerve fibre marker) and infrared spectral acquisition with Fourier-transform IR (ATR-FTIR) spectroscopy.

**Materials and Methods:** Immunohistochemical PGP 9.5 detection was performed according to Fraser group described methodology. PGP 9.5 stained fibers in functional endometrium were automatically counted with Image pro-plus in randomly selected 40X powerfields. Principal component-Linear discriminant analysis (PCA\_LDA) was used for chemometric analysis of the spectra acquired with a Bruker FTIR spectrometer

**Results:** Quantification of PGP 9.5 staining provided a best pair sensitivity/specificity of 83%/85% after ROC curve analysis. PCA-LDA analysis revealed an optimized sensitivity/specificity of 89%/81 for FTIR technology. Nerve fiber ranged from 0-1.25 to 0-31.25 fibers/mm<sup>2</sup> in the endometriosis group. In order to combine both approaches a cut-off point of 3.75 fibers/mm<sup>2</sup> (3 fold the maximal value in the control group) was employed for the correct segregation of all the control (100% specificity) and 15 out of 34 (44.5% sensitivity) endometriosis samples. The remaining 19 misclassified endometriosis samples were subsequently analyzed with FTIR spectroscopy which correctly classified as affected, 17 of them. After these two rounds of concatenated analysis the combined approach provided a best pair sensitivity/specificity of 94%/91%.

**Conclusion:** Nerve fiber detection had been previously described as a very sensitive technique for diagnosis endometriosis. In our hands PGP 9-5 was a very specific rather than sensitive technique. When appropriately combined with infrared spectroscopy, the global approach outperforms the specificity/sensitivity obtained with each individual technique separately

**Keywords:** P

Friday 2 May 2014

Seminar #7 - Non-invasive diagnosis

M7-5

HIGH FIDELITY GENOMIC CLASSIFIERS TO DIAGNOSE AND STAGE ENDOMETRIOSIS

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**Objectives:** To identify disease and severity diagnostic classifiers that distinguish with high accuracy women with endometriosis versus other uterine/pelvic conditions versus no disease through sequential binary decisions, each based on decision/classifier-specific sets of genes.

**Design:** Because the endometrial transcriptome differs in women with versus without disease, this study tested whether pelvic endometriosis can be diagnosed by endometrial tissue gene expression and subsequent margin tree classification and resampling techniques for construction, validation, and stratification of disease and severity diagnostic classifiers.

**Materials and Methods:** Endometrial transcriptomes of 144 women without/with endometriosis and/or other pelvic pathologies were analyzed using R/Bioconductor and margin tree classification and resampling techniques. Samples were partitioned into 80% construction/20% validation sets, with the former undergoing k-fold cross-validation to minimize overfitting. Validation sets computed classifier accuracy on samples not used during construction.

**Results:** A tree-like sequence of binary decisions based on specific genes distinguished: 1. presence or absence of uterine/pelvic pathology including endometriosis; 2. endometriosis/no endometriosis, and 3. minimal/mild or moderate/severe endometriosis. Best performing classifiers diagnosed endometriosis with 90-100% accuracy, were menstrual cycle phase-specific or independent, and utilized small numbers of genes to determine disease and severity.

**Conclusion:** Classifiers from high dimensional genomic data and margin tree analysis of endometrium can predict the presence/absence of pelvic pathology, if endometriosis is present, and stage of disease with high accuracy, suggesting endometrial analysis may replace surgical diagnosis. Furthermore, limited classifier candidate genes have high value for developing diagnostic/biomarker/therapeutic targets.

**Keywords:** Endometriosis diagnosis staging

Friday 2 May 2014

Seminar #8 - Management of deep disease

M8-1

**SEVERE URETERAL ENDOMETRIOSIS: PRELIMINARY REPORT OF 30 CASES WITH  
HYDRONEPHROSIS**

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**Objectives:** The objective is to describe perioperative management, complications and outcomes of severe ureteric endometriosis.

**Design:** Retrospective, descriptive study of patients who had surgery due to deep infiltrating endometriosis with hydronephrosis.

**Materials and Methods:** Consecutive patients who underwent laparoscopic surgery for hydronephrosis due to ureteral endometriosis (HUE) at the Department of Obstetrics and Gynecology, Strasbourg Hospitals; between June 2004 and June 2013.

**Results:** Two patients had non-functioning kidneys. Left ureteral lesions were more common (76.9%). Conversion was not necessary. Ureterolysis was performed in 10 patients (33.3%) and segmental resection-anastomosis in twenty (66,7%). All patients had improvement in pain symptoms. There were no intraoperative complications, but five major postoperative complications in four patients (13%).

**Conclusion:** HUE is a complex subset of patients presenting with a high possibility of ureteral resection and not negligible amount of complications. When managed in specialized team the outcomes are satisfactory, consequently it's critical to diagnose this condition preoperatively in order to offer the best standards of care and safety.

**Keywords:** Ureter hydronephrosis endometriosis

Friday 2 May 2014

Seminar #8 - Management of deep disease

M8-2

**ENZIAN CLASSIFICATION: DOES IT CORRELATE WITH CLINICAL SYMPTOMS AND THE ASRM SCORE?**

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**Objectives:** To assess the extent to which the Enzian classification correlates with the revised American Society for Reproductive Medicine (rASRM) score and clinical symptoms in patients with deeply infiltrating endometriosis.

**Design:** This is a retrospective cohort study.

**Materials and Methods:** Between January 1st, 2009 and December 31st, 2011, a total of 194 patients underwent surgery due to deeply infiltrating endometriosis. After histological confirmation, they were classified using the rASRM and Enzian systems. Clinical symptoms were recorded preoperatively. Endometriosis competence center specializing in minimally invasive surgery.

**Results:** A clear correlation was seen between grades of severity in the rASRM score and the Enzian classification ( $P < 0.001$ ). In addition, the rASRM severity grade and clinical symptoms correlated strikingly with the locations in the Enzian classification in relation to deeply infiltrating endometriosis. Pain and dysmenorrhea correlated strongly ( $P = 0.002$ ,  $P < 0.001$ ) with the severity grade in the Enzian classification.

**Conclusion:** In view of these clinical results, use of the Enzian classification can be recommended as a supplement to the rASRM score for detailed description of endometriosis.

**Keywords:** DIE; ASRM; Enzian

Friday 2 May 2014

Seminar #8 - Management of deep disease

M8-3

**ROBOTIC-ASSISTED LAPAROSCOPY FOR DEEP ENDOMETRIOSIS: INTERNATIONAL MULTICENTRIC RETROSPECTIVE STUDY**

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**Objectives:** To assess the interest of robotic-assisted laparoscopy in the context of deep infiltrating endometriosis and to investigate perioperative results.

**Design:** A multicentric retrospective study including 164 women with stage IV endometriosis who underwent robotic-assisted laparoscopy (DA VINCI Intuitive Surgical System®). Inclusions were made by eight international participating clinical centers from november 2008 to april 2012.

**Materials and Methods:** We evaluated the procedures performed, the duration of intervention, the complications, the recurrence and the impact on fertility.

**Results:** The average operative time was 180 minutes. The main complications were: 1 laparotomy (0.6%), 2 sutured bowel injuries (1.2%), 1 transfusion for a 2300ml bleeding, 1 case of prolonged urinary catheterization (0.6%), 1 uretero-bladder anastomotic leak (0.6%), 2 ureteral fistulas after ureterolysis (1.2%). The reoperation rate was 1.8% (n=3). The mean duration of follow-up was 10.2 months. 86.7% of patients had full recovery (n=98/113). 41.2% of patients (n=42/102) had a desire for pregnancy after surgery and 28.2% of them became pregnant (n=11/39).

**Conclusion:** This study is the largest series published in the literature on robotic-assisted laparoscopy for deep infiltrating endometriosis. The interest of robotic-assisted laparoscopy in deep infiltrating endometriosis was demonstrated while no increase in surgical time, blood loss, and intra- and postoperative complications were observed.

**Keywords:** Robotic-assisted laparoscopy

Friday 2 May 2014

Seminar #8 - Management of deep disease

M8-4

VALIDATING THE "ECOSYSTEM" FOR ENDOMETRIOSIS

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**Objectives:** Evaluate a new instrument designed to suggest the approach in patients with endometriosis, the "ECO-SYSTEM", within endometriosis patients of the Antonio Pedro University Hospital of Federal Fluminense University and an endometriosis center in Germany.

**Design:** A retrospective international and multicentric study. The records were collected and evaluated for complaints of patient and disease extent. A score from 0 to 2 is given for each of ECO SYSTEM criteria. The total score suggest how to manage the patient.

**Materials and Methods:** The criteria of "ECO SYSTEM" have been filled out and a score was obtained for each patient (The ECO-SYSTEM criteria are: E= extension of the endometriosis, C = complaints and O= objective of the patient.). This score indicated a suggested approach, which was compared with that adopted by the service.

**Results:** Of the 169 patients included in the study, 80 (48%) were conducted clinically versus 87 (52%) patients underwent surgical laparoscopy. Patients with score 2 were all subjected to clinical treatment, whereas scores 5 and 6 (n = 62) were all conducted in a surgical manner. In the group with score 3, fifty four (94.7%) were conducted clinically and three patients were surgically treated. In this study the variability in therapeutic decision was observed with the score 4 (n = 45), with 23 patients (51.1%) followed conservatively and 22 (48.9%) with surgical approach.

**Conclusion:** From this study, we emphasize the utility of the ECO system, which proved to be useful in predicting the conduct suggested by the endometriosis services. The score 4 represents the set point that allows the two conduits. Therefore, we propose a new score table and conduct for the ECO system.

**Keywords:** Endometriosis, management, classification

Friday 2 May 2014

Seminar #8 - Management of deep disease

M8-5

**ANATOMOPHYSIOLOGIC STUDY OF PATIENTS WITH PELVIC ENDOMETRIOSIS INTESTINAL INVOLVEMENT**

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**Objectives:** The purpose of this study was to evaluate the anatomy and function by tridimensional anorectal ultrasonography (3D US) and electromanometry (ARM) findings in women with intestinal endometriosis.

**Design:** Between April 2011 and August 2012, 39 female patients (mean age: 35,9) with rectal endometriosis diagnosed by 3D-US at coloproctology service (HospitalGenesis/Gastroclínica) were submitted to anorectal manometry (ARM) by two coloproctologists.

**Materials and Methods:** After this, all women were submitted a laparoscopy surgery by a team of gynecologists and surgeons. The 3D-US parameters evaluated included: injury to the internal and external anal sphincter. The ARM parameters evaluated included: resting pressure, squeeze pressure, straining, presence of relaxation reflex, rectal sensitivity and functional capacity rectal.

**Results:** The 3D-US showed no injury sphincter (sphincter internal and external). The 3D-US showed foci endometriosis, at least, on perirectal fat. The average pressure at rest was 59,59mmHg (normal: 40-70mmHg) the contraction of was 147,48mmHg (normal: 100-200mmHg). It was observed anismus ( absence of external anal sphincter and puborretal relaxation ) 18 (48,6%) patients and there was alteration of rectal sensitivity in 3 (8,1%) and of rectal capacity in 10 patients (27,0%).

**Conclusion:** We conclude that in patients with deep endometriosis with rectal involvement there was no incidence of injury sphincter and sphincter function was normal in most patients analyzed, but with considerable incidence of anismus.

**Keywords:** Anatomophysiologic; endometriosis intestina

Friday 2 May 2014

Session - Medical treatment

S4-1

**ARE WE FOLLOWING OUR NATIONAL ENDOMETRIOSIS CLINICAL PRACTICE GUIDELINES? A CANADIAN PERSPECTIVE**

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**Objectives:** To determine how well recommendations of the 2010 Society of Obstetricians and Gynecologists of Canada (SOGC) endometriosis clinical practice guidelines are being followed.

**Design:** Retrospective chart review of 250 consecutive women referred to a tertiary-care center specializing in the management of endometriosis over a 24-month period (2011-2012).

**Materials and Methods:** Medical records were reviewed and information on demographics, referral source/reason and previous medical/ surgical therapy was extracted and compared to the recommendations of the 2010 SOGC endometriosis clinical practice guidelines.

**Results:** Women with a mean age of 35 (range 16-51) years were referred by family physicians (26%) and gynecologists (74%). Referral reasons included pain (83%), infertility (6%), pain and infertility (6%) and asymptomatic mass (5%). For women with pain, 57% had tried at least one first-line agent (combined hormonal contraceptive or progestin) prior to referral; when a combined hormonal contraceptive was used, it was prescribed continuously in 29%. Second-line agents (GnRH agonist, Danazol or Levonorgestrel-IUD) were used by 49%; when GnRH agonists were prescribed, 37% received add-back therapy. For all women, 76% had prior endometriosis surgery of which 48% had not tried second-line medical therapy. During the most recent surgery, 38% had incomplete resection/ablation of disease. Endometrioma drainage was performed in 46% with a cyst  $\geq 3$ cm.

**Conclusion:** The recommendations of the SOGC endometriosis guidelines are not being consistently followed with respect to the medical and surgical management of disease. Continued education initiatives for healthcare professionals are necessary to standardize and improve the quality of care for women with endometriosis.

**Keywords:** Endometriosis, Canadian, Guidelines

Friday 2 May 2014

Session - Medical treatment

S4-2

**THE ASSOCIATION OF PYCNOGENOL WITH ORAL CONTRACEPTIVES FOR THE TREATMENT OF ENDOMETRIOSIS-RELATED PAIN**

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**Objectives:** Endometriosis is associated with persistent NF-Kappa.b activation. Progestins, on the other hand, are inhibitors of NF-Kappa.b translocation to cell nuclei, while pycnogenol acts by blocking post-translational events. This study investigated the combined effects of oral contraceptives (OC) and pycnogenol on the pain scores of endometriosis patients.

**Design:** The effect of the concomitant use of pycnogenol and OC in reducing pain scores was investigated in patients with laparoscopically diagnosed endometriosis using OC containing either gestodene or drospirenone in extended regimens. Pain scores were determined using a visual analog scale at baseline and 3 months later.

**Materials and Methods:** Forty-five women were allocated to one of four different treatment regimens: Group 1 (n=7) used an OC containing gestodene/ethinylestradiol (75/30 mcg); Group 2 (n=14) used the same OC with 100 mg of pycnogenol; Group 3 (n=13) used drospirenone/ethinylestradiol (3mg/30mcg); Group 4 (n=11) received drospirenone with 100 mg of pycnogenol.

**Results:** The use of OC alone (Groups 1 and 3) resulted in a significant decrease in mean pain scores from  $8\pm 1$  and  $7\pm 0.8$  to  $4\pm 1.4$  and  $4.3\pm 1.1$  [mean  $\pm$  standard deviation (SD) of the mean], respectively, after three months of treatment. However, in patients using OC + pycnogenol (Groups 2 and 4), mean pain scores decreased from  $7\pm 0.8$  and  $7.6\pm 0.5$  to  $0.5\pm 0.6$  and  $0.7\pm 1$  respectively, a significantly greater reduction than that found in Groups 1 and 3. On the other hand, there were no statistically significant differences in post-treatment pain scores between Groups 1 and 3 or between Groups 2 and 4. In pycnogenol users, 8/14 patients (57%) in Group 2 and 6/11 (54%) in Group 4 reported complete resolution of pain.

**Conclusion:** The combined administration of OC with pycnogenol, a post-translation inhibitor of NF-Kappa.b, resulted in a significantly greater decrease in endometriosis-related pain scores than that achieved with the use of oral contraceptives alone. This may constitute a new approach to increase the efficacy of hormonal treatment without increasing side effects.

**Keywords:** Pycnogenol, endometriosis

Friday 2 May 2014

Session - Medical treatment

S4-3

**UPDATE ON CHANGES IN BONE DENSITY IN WOMEN WITH SYMPTOMATIC ENDOMETRIOSIS DURING AND AFTER TREATMENT WITH LEUPROLIDE ACETATE AND NORETHINDRONE ACETATE**

Pamela Stratton<sup>1</sup>, Cassandra Charles<sup>2</sup>, Ninet Sinaii<sup>3</sup>, Jenny Anopa<sup>2</sup>, Mudar Dalloul<sup>2</sup>, Ozgul Muneyyirci-Delale<sup>2</sup>

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**Objectives:** To assess changes over time in bone mineral density (BMD) of women with endometriosis-associated pain undergoing treatment with leuprolide acetate (LD) compared with norethindrone acetate (NA).

**Design:** Prospective, double-masked clinical trial randomizing 62 women with symptomatic endometriosis to 24 weeks of treatment with 11.25 mg LD every 12 weeks or NA 5 mg daily (week 24), followed by 28 weeks of open-label NA daily (week 52) and then 12 months of follow-up (12 month FU).

**Materials and Methods:** Hip and lumbar spine BMD were measured at baseline, week 24, week 52 and 12month FU using DEXA (Delphi QDR Series, Hologic Inc). Change in BMD from each study phase to baseline were analyzed using paired t-tests or signed ranked tests adjusting for estrogen, BMI, age, and race, as appropriate.

**Results:** Women were predominantly Black (83%), between 21 and 47 years. Baseline lumbar and hip BMD (mean  $\pm$  SD, g/cm<sup>2</sup>) were similar (lumbar: 1.09  $\pm$  0.13 NA vs 1.09  $\pm$  0.11 LD; p=0.35 and hip: 0.99  $\pm$  0.09 NA vs 1.02  $\pm$  0.12 LD; p=0.11). After 24 weeks of LD, a significant decrease in lumbar (p<0.0001) and hip (p=0.0078) BMD compared to baseline occurred which persisted at week 52 (lumbar, p=0.0006; hip, p=0.0033) but recovered by 12 month FU (lumbar, p=0.75; hip, p=0.61). In contrast, lumbar or hip BMD for NA was unchanged at week 24 (lumbar, p=0.99; hip, p=0.31) or week 52 (lumbar, p=0.82; hip, p=0.037 trend for increased), with lumbar (p=0.012) but not hip (p=0.5675) significantly increased over baseline at 12 month FU.

**Conclusion:** Women taking depot leuprolide acetate for only 6 months experience bone loss that recovers slowly over time. In contrast to these women, women taking norethindrone acetate for endometriosis-associated pain experience an increase in bone mineral density and thus appear to be able to continue treatment for the long-term.

**Keywords:** Endometriosis; leuprolide; norethindrone

Friday 2 May 2014

Session - Medical treatment

S4-4

**AN ANTIPROGESTIN, CDB-4124, IMPACTS CYCLING AND HORMONES WHICH MAY LEAD TO ALLEVIATION OF SYMPTOMS OF ENDOMETRIOSIS**

Ronald Wiehle<sup>1</sup>, Michele Rosner<sup>1</sup>, Joseph Podolski<sup>1</sup>

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**Objectives:** Antiprogestins relieve pain in women with endometriosis. Antiprogestins trail antiestrogens in preclinical studies as modalities for the treatment of diseases. Antiestrogen therapies can have pernicious effects that can greatly reduce their acceptability. We carried out a trial to determine the effects of an antiprogestin on both estrogen and progesterone.

**Design:** A Phase II/III safety trial (ZP-204) to determine effects of an antiprogestin (CDB-4124 or Telapristone acetate) on cycling, hormones, and liver function.

**Materials and Methods:** Young women were recruited for a trial of various doses of CDB-4124 ranging from 1 mg to 12 mg per day. After a 4-week run-in period women were treated in one of five dose cohorts for 10 weeks. Liver enzymes were monitored weekly and cycling and hormones were followed periodically.

**Results:** At all doses at or above 3 mg per day, women appeared to be anovulatory with clearly no evidence of cycling at the higher doses as judged by ovulation kits and bleeding scores. Effects at low doses were unexpected. Hormone determinations show a dose-dependent lowering of serum estradiol after treatment and no evidence of luteal progesterone at the doses that were associated with amenorrhea. Periodic evaluations of drug in the serum confirmed that those women who were most affected also had measurable levels of drug or the main drug metabolite. Antiprogestin tended to increase endometrial thickness but not dose-dependently and without statistical significance. There were no signs of chronic liver injury

**Conclusion:** In such a low progesterone environment, antiprogestins may work optimally in lesions at the receptor level. Effects on women with endometriosis may be driven by changes in both steroids. Studies in women with endometriosis are being initiated at lower doses of CDB-4124.

**Keywords:** Endometriosis, antiprogestins, cycling

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Session - Medical treatment

S4-5

**PROTEIN KINASE INHIBITOR VEMURAFENIB CONTROLS THE PROGRESSION OF  
ENDOMETRIOSIS IN VITRO AND IN VIVO**

Pietro Santulli<sup>1</sup>, Veronique Boulard<sup>2</sup>, Sandrine Chouzenoux<sup>2</sup>, Carole Nicco<sup>2</sup>, Frederic Batteux<sup>2</sup>, Charles Chapron<sup>3</sup>

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**Objectives:** Mitogen Activated Protein Kinases (MAPKs) are involved in the proliferation and survival of endometriotic lesions. Vemurafenib is a novel protein kinase inhibitor targeting Braf, a member of the MAPKs pathway. The present study aims to test the effects of Vemurafenib on endometriotic cells in vitro and in vivo.

**Design:** We conducted a laboratory study in a tertiary-care university hospital, between September 2012 and September 2013. This study enrolled a cohort of 24 patients: 17 with histologically proven endometriosis and 7 unaffected women. A thorough surgical examination of the abdominopelvic cavity was performed in all study participants.

**Materials and Methods:** Ex vivo stromal and epithelial cells were extracted from endometrial and endometriotic biopsies from patients with and without endometriosis. Proliferation, apoptosis and pERK/ERK ratio were explored after treatment with Vemurafenib. Human endometriotic lesions were implanted in nude mice treated with vemurafenib during 2 weeks before sacrifice and histological examination.

**Results:** Treating endometriotic cells with 25 µM of Vemurafenib abrogated the phosphorylation of ERK with a significant reduced pERK/ERK ratio in both epithelial and stromal cells of endometriotic women as compared to controls ( $p < 0.01$  and  $p < 0.05$ , respectively). In addition after treatment with Vemurafenib we found significant decreased proliferation in both stromal and epithelial cells with concomitant increase of cellular apoptosis. Human endometriotic ectopic samples were grafted in 10 NUDE mice. After randomization 5 mice were treated with intraperitoneal Vemurafenib (25mg/kg/day) whereas 5 were treated with placebo. After two weeks treatment with Vemurafenib the initial size of the implants was significantly decreased ( $8.2 \pm 1.1$  vs  $6.2 \pm 0.9$ , respectively;  $p < 0.05$ ). In striking contrast mice treated with placebo failed to show any change in implant size ( $7.9 \pm 0.6$  vs  $8.9 \pm 1.1$ , respectively;  $p = 0.274$ ).

**Conclusion:** Our data suggest that MAPKs and Braf are involved in the pathogenesis of endometriosis. The inhibition of the Braf protein kinase using Vemurafenib controls the growth of endometriosis in vitro and in vivo.

**Keywords:** Vemurafenib, endometriosis, MAPK

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Session - Medical treatment

S4-6

**LONG TERM TREATMENT WITH LETROZOLE AFTER GNRHA DOWN REGULATION IN  
PREMENOPAUSAL WOMEN WITH MODERATE AND SEVERE ENDOMETRIOSIS. A SAFETY AND  
EFFICACY STUDY**

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**Objectives:** The use of aromatase inhibitors (AI) has long been advocated for the treatment of endometriosis, but the effect of long term AI monotherapy in premenopausal women is unknown. We compared the safety, tolerability and efficacy of letrozole after down regulation with the GnRHa leuprorelin acetate.

**Design:** Multicenter, open-label, exploratory phase II randomized controlled trial (RCT)

**Materials and Methods:** 40 premenopausal women with moderate/severe endometriosis received two months GnRHa-pretreatment before randomization (N=36) to 4 months treatment of letrozole 2.5mg/day (N=19) or GnRHa 3.75mg/month (N=17). Safety variables included adverse event profile, gynaecological and ultrasound examination and laboratory parameters. Efficacy was assessed by pain reduction using the visual analog scale (VAS)

**Results:** Five SAEs in the letrozole group - arthralgia, large ovarian cysts, vaginal bleeding, low abdominal pain - led to premature discontinuation and were considered to be related to the study medication. Under GnRHa treatment a significant decrease of LH (p=0.018), estradiol (p=0.028), estrone (p=0.036), progesterone (p=0.046) and cortisol (p=0.043) and Ca125 (p=0.012) levels were observed. However, in the letrozole group only estrone levels were significantly reduced (p=0.047), whereas a significant increase of LH (p=0.001), FSH (p=0.033), estradiol (p=0.006), progesterone (p=0.015) and Ca125 (p=0.036) was observed. In the letrozole group 13 patients developed new functional cysts >3cm, but none in the GnRHa group. The VAS pain score decreased significantly under GnRHa treatment (p=0.005) but showed an increase under letrozole treatment.

**Conclusion:** The suppression of estrone alone under letrozole treatment is insufficient to achieve a sustainable pain relieve and the frequent development of large functional cysts and SAEs leading to a premature discontinuation of treatment suggest, that long-term letrozole monotherapy is unsafe in premenopausal women and inefficient for the treatment of endometriosis.

**Keywords:** Endometriosis, aromatase-inhibitor, premenopause

Friday 2 May 2014

Session - Medical treatment

S4-7

**EVALUATION OF THE EFFICACY OF TWO DIFFERENT ORAL CONTRACEPTIVE FORMULATIONS ADMINISTERED IN A CONTINUOUS FASHION FOR MODERATE TO SEVERE DYSMENORRHEA: PRELIMINARY RESULTS.**

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**Objectives:** Evaluate the efficacy of two different oral contraceptive formulations, one containing 20 µg of etinilestradiol (EE) and 100 µg of levonorgestrel (LNG) (group 1) and the other with 30 µg of EE and 150 µg of LNG (group 2).

**Design:** This is an open label, randomized clinical trial.

**Materials and Methods:** After 6 months of treatment visual analog scales were used to assess dysmenorrhoea, dyspareunia and non-menstrual pain. The Short-Form 36 survey instrument (SF-36) was used to assess quality of life and the Beck Depression Inventory (BDI) was used to measure depression. Adverse events and bleeding episodes were also recorded.

**Results:** Until now 8 patients from group1 and 10 from group 2 completed the study. There was no statistical difference between the two groups on SF-36 or BDI questionnaires after six months of treatment. Bleeding episodes were similar between groups. When both groups were analyzed together, there was a significant reduction from baseline dysmenorrhoea ( $p<0.0001$ ), dyspareunia ( $p<0.04$ ) and non-menstrual pain ( $p<0.006$ ). Important improvement on quality of life domains of SF-36 and reduction on 8 out of 12 of BDI were observed. There were no major adverse events in both groups.

**Conclusion:** Both formulations were very effective in the management of moderate to severe dysmenorrhea. An improvement in quality of life measurements was also seen. There were no more bleeding episodes with the lower dose of EE. Lower dose of EE maybe be a better option, especially with continous long term use.

**Keywords:** Dysmenorrhea, oral contraceptive

Friday 2 May 2014

Session - Diagnosis and screening

S5-1

**THE ROLE OF THE GENERAL PRACTITIONER IN THE DIAGNOSTIC PROCESS OF DUTCH WOMEN WITH ENDOMETRIOSIS**

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**Objectives:** The goal of this study was to identify the time to diagnosis of endometriosis in Dutch women and the role of the General Practitioner (GP) in this process.

**Design:** A questionnaire was sent to the members of the Dutch Endometriosis Society (ES). On the basis of the results of this questionnaire, advices for improvement of the diagnostic process of endometriosis may be formulated.

**Materials and Methods:** A descriptive study was conducted among members of the ES who had an email address (n=839). They received a questionnaire consisting of 62 multiple choice questions via email using Pontifexsurvey.nl, a commercial data processing company. Statistics were calculated using Excel for Windows.

**Results:** 349 (42%) women responded to the questionnaire (42%). 13 women were excluded. Age at onset of complaints was 16.7 yrs (SD 6.4). Women visited their GP after 5.3 years (SD 6.8) of complaints. In 52%, another diagnosis than endometriosis was considered first, and in 30.1% treatment for a different disease was initiated, mainly for gastro-intestinal diseases (74.3%). Initial management included referral (29.8%), hormonal medication 25.9%, pain medication (22.0%), lifestyle advices (13.7%), expectant management (3.9%), or other options (8.6%). After 7.8 years (SD 7.6) after initial contact with the GP, patients were referred. Diagnosis was made after 13.1 years after initial complaints. Women visited a number of 2.0 GPs (SD 1.1) and 2.4 (SD 1.8) specialists before diagnosis.

**Conclusion:** Doctors delay in the diagnosis of endometriosis in Dutch women is 7.8 years. This is the first report describing the diagnostic process in Dutch women with endometriosis in an unselected population. GPs should be educated to accelerate the diagnostic process by considering endometriosis in an earlier stage.

**Keywords:** General practitioner, Diagnosis

Friday 2 May 2014

Session - Diagnosis and screening

S5-2

**DELAY IN CLINICAL DIAGNOSIS OR DELAY IN REFERRAL FOR ADEQUATE TREATMENT: WHICH HAS A GREATER IMPACT ON THE MANAGEMENT OF ENDOMETRIOSIS?**

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**Objectives:** To evaluate the decision making of gynecologists in a clinical setting regarding the diagnosis and management of endometriosis.

**Design:** A qualitative questionnaire based study

**Materials and Methods:** During two local meetings of gynecologists, participants were asked to fill out a 16 item questionnaire regarding the diagnosis and management of endometriosis. Participants were gynecologists in a community and a hospital setting.

**Results:** Physician's reported management and treatment methods. The questionnaire was answered by 91 gynecologists. Most had at least 10 years of clinical experience (72.2%), 37.8% were community based, and 5.6% were ultrasound experts. Approximately 62.8% of physicians believe that there is delayed diagnosis of endometriosis. Most would refer the patient to a specialized endometriosis center in the presence of a large pelvic mass, following repeated IVF failure, or due to intractable pain after repeat surgery. Physicians' seniority or subspecialty did not significantly influence their opinions.

**Conclusion:** It seems that it is not delayed clinical diagnosis that affects the management of endometriosis, but rather delayed referral to targeted investigation and appropriate treatment. Gynecologists in community practice are still largely unaware of the role of specialized care in the management of endometriosis.

**Keywords:** Endometriosis, diagnosis, delay

Friday 2 May 2014

Session - Diagnosis and screening

S5-4

**EVALUATION OF THE BIOMARKER HE4 AS A DIFFERENTIAL TOOL IN PATIENTS WITH DIFFERENT STAGES OF ENDOMETRIOSIS AND OVARIAN CANCER.**

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**Objectives:** Differentiation between endometriosis and ovarian cancer(OC) is essential for the optimal patient referral. Human epididymal secretory protein E4(HE4) is a new promising tumor marker in differentiating endometriotic cysts from malignant disease. The aim of this study was to evaluate HE4 in relation to different stages of endometriosis and OC.

**Design:** A prospective ongoing study with the objectives to identify diagnostic and prognostic factors in women with a pelvic mass. The participants were included when admitted for surgery due to a pelvic mass or pelvic pains. In the present study only participants below 50 years of age were included.

**Materials and Methods:** 265 patients with endometriosis with stadium 1-4 endometriosis, 252 patients with benign pelvic masses, 22 patients with borderline tumors and 41 patients with OC were included. Serum concentrations of HE4 and CA125 were measured and the ovarian malignancy algorithm (ROMA) and risk malignancy index (RMI) were calculated.

**Results:** The median HE4 concentrations in endometriosis patients were 45 pmol/L (range: 19-379), in other benign pelvic masses 48 pmol/L (range: 23-1364), in borderline tumors 62 pmol/L (range: 29-495) and in OC 205 pmol/L (range: 16-8816) ( $p < 0.0001$ ). No correlation was observed between HE4 and different stages of endometriosis ( $\rho = 0.046$ ,  $P = 0.752$ ) in contrast to CA125 ( $\rho = 0.463$ ,  $P < 0.0001$ ). Using receiver operating curve (ROC) analysis comparing endometriosis with OC revealed that HE4 could discriminate between the two conditions with a sensitivity of 90.2 and a specificity of 78.1 ( $p < 0.0001$ ) using a cut-off value of 60 pmol/L. The area under the ROC curve (AUC) was found to be 0.89 for HE4, which was not significantly different from the AUC of CA125, RMI and ROMA.

**Conclusion:** We found no correlation between HE4 and the stage of endometriosis whereas a significant association with CA125 was observed. HE4 appears to be a potential good biomarker to differentiate between endometriosis and ovarian cancer, but it did not perform significantly better than CA125, ROMA or RMI.

**Keywords:** endometriosis, HE4, ROMA

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Session - Diagnosis and screening

S5-5

**COMPARISON BETWEEN TRANSVAGINAL ULTRASOUND WITH BOWEL PREPARATION AND PELVIC MAGNETIC RESONANCE IMAGING FOR THE DIAGNOSIS OF DEEP ENDOMETRIOSIS**

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**Objectives:** The objective of this study was to evaluate the capacity of transvaginal ultrasound with bowel preparation (TVUS) and magnetic resonance imaging (MRI) to diagnose rectosigmoid involvement due to endometriosis.

**Design:** We conducted a prospective study.

**Materials and Methods:** From July 2009 to July 2013, a total of 200 patients with clinically suspected endometriosis were submitted to clinical examination (vaginal exam), pelvic MRI and TVUS at least 3 months prior to videolaparoscopy and the findings of these methods were matched with laparoscopical and histopathological confirmation of endometriosis.

**Results:** Endometriosis was histologically confirmed during laparoscopy in 198 of 200 (99%) patients. Regarding to the rectosigmoid, retrocervical and ureteral sites, we evaluated sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV), respectively. TVUS had a sensitivity of 99, 96 and 94%, specificity of 100, 98 and 96%, PPV 100, 98 and 98%, NPV of 99,98 and 96%. MRI had a sensitivity of 80, 74 and 78%, specificity of 96, 68 and 62%, PPV of 98, 94 and 60% and NPV of 82, 74 and 80%.

**Conclusion:** TVUS when performed by a skilled examiner, had better sensitivity, specificity, PPV, and NPV to the diagnosis of deep ureteral, retrocervical and rectosigmoid endometriosis when compared with MRI, demonstrating that it is a very important preoperative evaluation to define surgical strategies.

**Keywords:** endometriosis, MRI, ultrasound

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Session - Diagnosis and screening

S5-6

**THREE-DIMENSIONAL RECTOSONOGRAPHY: DESCRIPTION AND EVALUATION OF A 3D TRANSVAGINAL ECHOGRAPHY WITH CONTRAST TO ASSESS COLORECTAL ENDOMETRIOSIS**

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**Objectives:** In this study, we describe a new technique, combining classical transvaginal ultrasonography (TVUS), 3-dimensional (3D) ultrasonography and rectal contrast by water, called 3D rectosonographie (3D-RSG). We also assess the feasibility and the diagnostic performance of this technique.

**Design:** Prospective mono centric Longitudinal study

**Materials and Methods:** Patients were selected on the presence of symptoms suggestive of DIE. After colorectal enema, patients underwent a gynecological examination and an TVUS. Then an intra-rectal injection of 120 ml of water was done to improve the performance of the examination.

**Results:** 50 patients underwent 3D-RSG between April and July 2012. All procedures were well tolerated by patients. 2 exams (4%) were stopped for technical reasons. Eighteen rectosigmoid nodules were diagnosed in 17 patients (34%). Seventeen of the 18 digestive's nodules were also diagnosed with MRI, and one nodule seen on MRI was not diagnosed by 3D-RSG. Thirty-one examinations showed no digestive lesions using either technique. We found sensitivity, specificity, positive and negative predictive value of 0.95, 0.97, 0.95 and 0.97 respectively.

**Conclusion:** 3D-RSG is a new powerful method for diagnosis of rectosigmoid endometriosis which is also feasible and well tolerate. We propose to perform a first line 3DRSG whenever the diagnosis is suspected, although further studies are needed to confirm.

**Keywords:** Rectosigmoid endometriosis, 3D ultrasonography

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Session - Diagnosis and screening

S5-7

### EVALUATION OF PLASMA MICRORNAS AS DIAGNOSTIC BIOMARKERS FOR ENDOMETRIOSIS

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**Objectives:** Surgery is the only method of definitively diagnosing endometriosis; however, it is risky, costly and associated with considerable diagnostic delay. Our aim was to identify circulating microRNA (miRNA) biomarkers for endometriosis and evaluate their value as a diagnostic test in 2 large, independent, surgically-defined populations of women with endometriosis symptoms.

**Design:** Plasma microRNAs identified as deregulated in women with endometriosis, were measured in a prospective cohort of surgically defined, endometriotic and endometriosis-free women with pelvic pain (n=78). The diagnostic accuracy of 6 plasma microRNAs was further evaluated in an independent test cohort of similar, surgically diagnosed women (n=118).

**Materials and Methods:** Taqman Low Density RT-PCR arrays identified 33 endometriosis-associated, plasma microRNAs. RT-PCR measured these plasma microRNAs in 78 symptomatic women undertaking diagnostic surgery. Six significantly deregulated plasma microRNAs were further evaluated by RT-PCR in an independent test cohort. Receiver operating curves were generated for significantly deregulated miRNAs individually and in combination.

**Results:** The Taqman array analyses identified 33 endometriosis-associated plasma miRNAs and 8 candidate reference miRNAs. In the initial cohort, 6 miRNAs (miR-574-3p, miR-155, miR-29c, miR-100, X and Y) were differentially regulated in women with endometriosis (p<0.05). In the test set, expression levels of miR-574-3p, miR-155 and X were significantly altered in women with endometriosis (p values = 0.031, 0.046 and 0.005, respectively). The area under the ROC curve was 0.72 in the multivariate analysis of these 3 miRNAs. Using a cut-off of 0.612 (relative expression in comparison to miR-30b), these miRNAs distinguished endometriosis and control subjects with a sensitivity of 79% and a specificity of 51%. Menstrual cycle phase or a history of alternate disease did not influence plasma miRNA expression levels. (\* will be disclosed)

**Conclusion:** Plasma microRNAs were identified as differentially expressed in endometriosis. Although a diagnostic algorithm, using the 3 most promising plasma miRNA, did not confer the sensitivity and specificity necessary to formulate an isolated definitive diagnostic test, these microRNAs could contribute to future diagnostics in combination with other endometriosis biomarkers.

**Keywords:** endometriosis, microRNAs, biomarkers.

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Session - Immunology and stem cells

S6-1

**NERVE REPELLENT FACTORS AFFECT THE INFLAMMATORY CONDITION OF ENDOMETRIOSIS**

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**Objectives:** The main symptom of EM is pelvic pain, often accompanied by chronic inflammation. EM affected tissue shows decreased levels of noradrenergic (NA) anti-inflammatory nerve fibers (NF), which seems to play a crucial role in the inflammatory condition in EM. The mechanisms underlying the reduction of NA-NF in EM, remains unclear.

**Design:** Semaphorins are factors able to repel NF; studies have shown an involvement of semaphorins in NF modulation in many chronic inflammatory diseases. In order to characterize the role of semaphorins in EM, the expression of semaphorins and their receptors was analysed. Additionally, possible interactions between semaphorins and macrophages were studied.

**Materials and Methods:** Immunohistochemical staining of semaphorins 3C/3F and neuropilin 1/2 was performed. Furthermore, the expression of macrophages was analyzed and an immunohistochemical double staining served to determine, if macrophages express semaphorins. All experiments were each performed in 40 peritoneal endometriotic tissue (PET) and 10 peritoneal tissue from women without EM (PT).

**Results:** Semaphorins 3C and 3F are expressed in a variation of cells near the EM lesions, including the stroma and epithelial cells of EM lesions, but also in further still not characterised cells. The expression of semaphorins 3C and 3F is significantly increased in PET when compared to the expression in PT of patients without EM. The receptors neuropilin 1 and 2 could be identified in stromal and epithelial cells near the EM lesions, but also in vessels and NA-NF in PET. The density of macrophages in PET is significantly higher in comparison to density levels in PT from women without EM, and most of the macrophages found in PET expressed semaphorins 3C and 3F, but not the macrophages in PT from patients without EM.

**Conclusion:** The chronic pro-inflammatory reaction in EM inducing a macrophages release is crucial for its pathogenesis. EM-associated macrophages and further cells expressing semaphorins are potentially involved in the reduction of NA-NF and consequently of an impairment of anti-inflammatory neurotransmitters in PET thereby supporting the chronic inflammatory condition in EM.

**Keywords:** Endometriosis, chronic-inflammation, semaphorins

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Session - Immunology and stem cells

S6-2

**CHARACTERIZATION OF THE SUBPOPULATIONS OF TOPIC ENDOMETRIOTIC TISSUE – A PUTATIVE ENDOMETRIOTIC STEM CELL POPULATION?**

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**Objectives:** This work aims at characterizing all the subpopulations of the topic endometrium of women with endometriosis stage IV.

**Design:** The topic endometrium tissue of five patients with endometriosis stage IV was surgically collected and the cell pool obtained after tissue digestion was submitted to an isopycnic fractioning (discontinuous density gradient).

**Materials and Methods:** All the fractions obtained were cultured in treated culture plates for at least 2 doubling cycles and then characterized with flow cytometry for the following markers: CD9, CD13, CD29, CD34, CD56, CD73, CD90, CD105, CD146.

**Results:** These analyses showed at least 5 different populations in the topic endometrium, including the already known glandular and stromal fractions as well as less differentiated cells (CD9-CD13-). These cells were enriched in the fractions 1, 5, 6 and 7 of the density gradient. Most of the cells were collected at grade 4 ( $d \cong 1,058\text{g/L}$ ). The majority of them were CD13+CD9+ and CD9-CD13-. About 40% of this fraction population presents a classical mesenchymal stem cell profile (CD29+ CD73+ CD90+ CD105+). In the fraction 6 ( $d \cong 1,035\text{g/L}$ ) there was enrichment in the CD146+ population, already characterized in the healthy endometrium as highly proliferative and with mesenchymal lineages differentiation capability, and also in the CD29+CD34-CD56+CD90+ population, suggesting a different mesenchymal cells population from that found in fraction 4.

**Conclusion:** The great number of cells without any of the tested markers expression as well as the presence of two putative different mesenchymal cells populations indicate that the endometriotic endometrium have at least 2 different stem cells populations which could be involved in the development of the disease.

**Keywords:** Endometriosis-stage-IV, Stem-cells, Mesenchymal-cells.

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Session - Immunology and stem cells

S6-3

**REGULATORY T CELLS IN ENDOMETRIOSIS: POTENTIAL ROLES IN PATHOGENESIS**

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**Objectives:** To investigate regulatory T cells (Tregs) in endometriosis. Regulatory T cells are a sub-population of T cells which control and suppress immune responses. It has previously been indicated that Treg populations are disturbed in women with endometriosis, however the details and their roles in the disease are currently unclear.

**Design:** In this ongoing case-control study, reproductive-age women with and without endometriosis are recruited from gynaecology operating theatres at Royal Prince Alfred Hospital, Sydney. Women on hormonal or immunosuppressive therapy, with a history of autoimmune disease or recent infection are excluded. Blood and endometrial samples are collected to study Treg populations.

**Materials and Methods:** Samples are prepared as single cell suspensions, labelled with a fluorescent dye to discriminate live and dead populations and stained with an antibody cocktail for Treg detection (Treg Detection Kit; Miltenyi Biotech). The cocktail contains fluorescent-conjugated monoclonal antibodies against standard Treg cell markers. Tregs are quantified by multi-colour flow cytometry.

**Results:** Preliminary results from women with (n=15) and without endometriosis (n=5) show the presence of CD4+CD25+CD127dim Tregs with proportions ranging from 2.9-6.6 % of CD4+ cells in blood and 4.9-44.4 % in endometrium. In endometrium, Treg proportions in the secretory phase appear to be higher in women with endometriosis (mean±SD = 15.0±12.3% of CD4+ cells) compared to women without (11.0±6.2%). There are menstrual cycle-dependent changes in Treg populations in blood and endometrium. Endometrial Tregs appear to increase progressively from menstruation through to the secretory phase in women with endometriosis (6.5 vs 15.0±12.3% of CD4+ cells, respectively), while proportions in the blood are highest during the proliferative phase (6.0±2.8%, compared to 3.4% and 4.8±1.8% of CD4+ cells in menstruation and the secretory phase, respectively).

**Conclusion:** This study indicates that circulating and endometrial Tregs may be altered in endometriosis. Recruitment is continuing comprehensively to characterise Tregs in endometriosis and elucidate immune dysregulation aspects of pathophysiology. Tregs are crucial for female fertility and understanding their disturbance in endometriosis may therefore also shed light on endometriosis-associated infertility.

**Keywords:** Endometriosis, Endometrium, Tregs

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Session - Immunology and stem cells

S6-4

**THE ENDOMETRIAL STEM CELL MARKERS NOTCH AND NUMB ARE ASSOCIATED WITH ENDOMETRIOSIS**

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**Objectives:** Aberrant stem cell function may contribute to the pathogenesis of endometriosis. The stem cell markers Notch-1 and Numb are cell fate determinants affecting proliferation, differentiation and apoptosis. Our objective was to study a potential association of Notch-1 and Numb expression with endometriosis.

**Design:** Immunohistochemical correlation study using eutopic endometrium of patients with laparoscopically confirmed endometriosis and a control collective.

**Materials and Methods:** 64 female patients with endometriosis were compared with 101 disease-free controls in the IVF unit and the tertiary endometriosis referral centre of Münster university hospital. Endometrial biopsies were immunostained for Notch-1 and Numb and staining was correlated with clinical data prospectively collected over 3 years.

**Results:** Numb expression in the luminal epithelium was significantly higher in eutopic endometrium of patients with endometriosis and with peritoneal endometriosis compared with controls (20.5% vs. 16.5% and 19.9% vs. 16.5%; P=0.033 and P=0.046; respectively). Numb staining of stromal cell nests was more frequent and single stromal cells were less frequent in patients with an endometrioma compared to other forms of endometriosis (0.3 vs. 0.2 and 0.3 vs. 0.5; P=0.024 and P=0.028; respectively). Notch-1 expression in endometrial glands was significantly higher in patients with deep infiltrating endometriosis compared with controls (39.1% vs. 21.8%; P=0.045).

**Conclusion:** This study contributes novel evidence to the hypothesis that stem cells are involved in the etiology of endometriosis, possibly contributing to the variable clinical phenotypic presentation of the disorder. In future, these findings could help to develop promising research strategies applying endometrial stem cell as novel diagnostic and therapeutic tools.

**Keywords:** Eutopic, notch, numb

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Session - Immunology and stem cells

S6-5

**CYTOKINE RELATED TO NATURAL KILLER AND T-REGULATORY CELLS HAVE A DIFFERENT PROFILE IN DEEP ENDOMETRIOSIS**

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**Objectives:** As demonstrated in previous studies, natural killer and T-regulatory cells have higher concentrations, respectively, in blood and peritoneal fluid in women with endometriosis when compared to those without the disease. The objective of this paper is to evaluate cytokines related to these cells in lesions of patients with deep endometriosis.

**Design:** It was performed a prospective study in a tertiary referral hospital. Sixty-four consecutive patients underwent videolaparoscopy and were divided into 2 groups: deep infiltrative endometriosis (n=32) and endometriosis-free women (n=32). Eutopic endometrium was collected from both groups and endometriotic lesions were collected from endometriosis patients.

**Materials and Methods:** The concentration of IL-2, IL-4, IL-7, IL-10, IL-12, IL-15, TGFβ1 and IFNγ was estimated using a Luminex® multiplex suspension bead array in eutopic endometrium of both groups and in endometriotic lesion. Kruskal-Wallis test and multiple comparisons non-parametric Dunn and Mann-Whitney tests were performed to analyze the data.

**Results:** IL-2, IL-10, TGFβ1 and IFNγ had significantly higher concentrations in the eutopic endometrium in the control group (p<0.05) when compared with either the eutopic or ectopic endometrium in the endometriosis group. Cytokines IL-4 and IL-15 were also noted to be significantly lower in the eutopic endometrium in the control group compared to the other groups (p<0.05). Concerning IL-7, this cytokine had lower concentration in the control group when compared to the eutopic endometrium of the endometriosis group (p<0.05) and no differences were observed when compared to the endometriotic lesions (p>0.05). Finally, IL-12 showed no differences between the 3 groups (p>0.05).

**Conclusion:** Cytokines related to T-regulatory and Natural Killer cells presented different concentrations in deep endometriotic lesions and these results show that the activity of these cells may be modified. These modifications may help the understanding of endometriosis pathogenesis.

**Keywords:** Endometriosis, immunology, cytokine

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Session - Immunology and stem cells

S6-6

**DENDRITIC CELLS, THE MENSTRUAL CYCLE AND ENDOMETRIOSIS: CIRCULATING AND ENDOMETRIAL POPULATIONS**

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**Objectives:** To comprehensively characterise dendritic cell (DC) sub-populations in women with endometriosis. Immune cells, including DCs, have been implicated in pathogenesis of endometriosis but this is not well understood. There are two main DC sub-types, myeloid (mDC) and plasmacytoid (pDC), crucial for initiating and regulating both innate and adaptive immune responses.

**Design:** Women of reproductive-age with and without endometriosis are being recruited from gynaecology operating theatres at Royal Prince Alfred Hospital (Sydney) in this ongoing study. Exclusion criteria include hormonal or immuno-suppressive therapy, or history of autoimmune disease or recent infection. DC populations are characterised in blood and endometrial samples.

**Materials and Methods:** Samples are stained for identification of DC populations by multi-colour flow cytometry. DC are identified by lack of common lineage marker expression (CD3,14,19,20,56) and positive HLA-DR expression. Based on the current international consensus on DC nomenclature, three CD11c+ mDC (CD1c+, CD141+, CD16+) and two CD304+ pDC (CD2+/-) populations are assessed.

**Results:** Preliminary blood results (endometriosis=11, control=3) show variation in DC populations during the menstrual cycle. During the proliferative phase mDC proportions appear to be decreased in women with endometriosis (mean  $\pm$  SD = 42.6  $\pm$  17.4% vs. 56.8  $\pm$  6.2% of Lin-HLADR+ cells) while pDC are increased (22.0  $\pm$  15.2% vs. 11.9  $\pm$  11.5%). Optimisation of complex analysis of DCs in endometrium (endometriosis=8, control=1) has shown for the first time that all three mDC and both pDC sub-populations are present. Preliminary results demonstrate higher proportions of mDC than pDC in the endometrium (42.4  $\pm$  15.6% vs. 22.1  $\pm$  15.8%, respectively). DC proportions in endometrium in endometriosis vary during the menstrual cycle, with mDC appearing to be greatest during the secretory phase while pDC peak during menstruation.

**Conclusion:** Blood and endometrial DC populations appear to be disturbed in endometriosis. Cyclical variations in DCs suggest recruitment from circulation into the uterus and involvement in signalling and functional changes of the uterus. Differences in endometriosis point to these processes being disturbed in these women. This study is ongoing.

**Keywords:** Dendritic cells, pathogenesis

Friday 2 May 2014

Session - Immunology and stem cells

S6-7

**EXPRESSION OF ANGIOTENSIN RECEPTORS TYPE1(AT1),TYPE2(AT2) MRNA IN LOCAL  
ENDOMETRIOSIS LESIONS**

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**Objectives:** The presence of angiotensin receptors has been demonstrated in the endometrial tissue. Angiotensin $\alpha$  receptors can be classified angiotensin (AT) 1, AT2 and non AT1/AT2 receptors. Angiotensin $\alpha$  in endometrial stromal cells was mediated via AT1 receptor. We investigated into the expression of AT1, AT2 receptors in local lesions of endometriosis.

**Design:** An experimental study of the expression of AT1, AT2 mRNA in local endometriosis lesions.

**Materials and Methods:** Endometriosis samples were obtained from 35 patients of endometrial cyst. Endometrial tissues were obtained from patients undergoing operations for benign gynecological conditions. Tissue samples were stored at -80 C° until analysis. The expression of AT1, AT2 receptors mRNA was measured by real-time reverse transcription-polymerase chain reaction.

**Results:** The expression level of AT1 receptors mRNA of secretory phase was significantly higher than that of proliferative phase in non-endometriosis control. The expression level of AT1 receptors mRNA of endometriosis sample was significantly increased compared to eutopic proliferative endometrium of non-endometriosis control. There was a relationship between expression of AT1 receptor mRNA and COX-2 mRNA in endometriosis samples.

**Conclusion:** The expressions of AT1, AT2 receptors mRNA of endometriosis samples indicate that RAS may play an important role in the pathogenesis of endometriosis.

**Keywords:** Endometriosis, Angiotensin receptors.

Friday 2 May 2014  
Session - Quality of life

S7-1

**PERSONALITY CORRELATES OF ENDOMETRIOSIS**

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**Objectives:** To examine psychosocial variables that characterize patients diagnosed with endometriosis as compared with matched healthy controls, so as to identify factors likely to play the role of psychological risk factors for endometriosis. The theoretical background of the study was the cognitive orientation theory of disposition for physical health disorders.

**Design:** The study was based on a multi-factorial two-group design known as causal-comparative design.

**Materials and Methods:** The participants were 80 women diagnosed with endometriosis and 80 healthy women, matched to the patients' group in age, ethnic background, and in educational, occupational and marital status. They were administered a questionnaire of demographic and medical information and the Cognitive Orientation Questionnaire of Endometriosis assessing personality tendencies and attitudes.

**Results:** The major psychological variables – four kinds of beliefs and five theme factors – differentiated significantly between the two groups. Endometriosis patients scored higher in all variables, as hypothesized. A regression analysis yielded a highly significant prediction ( $p < .001$ ) of membership in the endometriosis or healthy group. The major psychosocial variables characterizing endometriosis patients were tendencies to conform to regulations, feelings ones' strength and power, emotional withdrawal, social dissociation, striving for perfectionism and independence, and high achievement motivation. Notably, some of the psychological tendencies define specific sources of conflict and stress.

**Conclusion:** There are unique psychological correlates characteristic of endometriosis. Endometriosis may be affected to some extent by specific psychological tendencies of the patients. It is suggested that psychological adjuvant interventions accompany the medical treatment of the disorder. Future research is warranted for identifying specific psychological risk factors for endometriosis.

**Keywords:** Endometriosis, psychological, stress

Friday 2 May 2014

Session - Quality of life

S7-2

**ENDOMETRIOSIS IMPACT QUESTIONNAIRE (EIQ): NEW QUESTIONNAIRE TO MEASURE LONG TERM IMPACT OF ENDOMETRIOSIS ON WOMEN'S LIVES**

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**Objectives:** Endometriosis is a chronic condition that can impact on many aspects of a woman's life. Current endometriosis impact tools measure recent (within four weeks) disease impact. We are developing the Endometriosis Impact Questionnaire (EIQ) to measure the long term impact of endometriosis during the whole course of the disease.

**Design:** This study is methodological research. First we explored women's experiences of the impact of endometriosis through conducting 10 focus group discussions with 35 women with endometriosis. Secondly, we developed the EIQ questions based on themes that arose from the focus groups.

**Materials and Methods:** First draft of the EIQ had 100 questions. Experts and endometriosis patients assessed face validity and rated the EIQ items based on 'Relevance', 'Clarity' and 'Simplicity'. 350-400 women with endometriosis are being recruited to complete the EIQ, demographic section and EHP-5 (Jones, et al, 2004) either online or paper version.

**Results:** 14 experts and 12 patients assessed content and face validity of EIQ. Scale Content Validity Index was 0.84 and 0.93 from the experts and patients' view respectively. Current EIQ has 66 items ranked using a 5 point likert scale including "Not at all", "A little", "Somewhat", "Quite a lot", and "Very much". The EIQ asks women about how much endometriosis has affected their lives over last 12 months, 1 to 5 years ago and more than 5 years ago through seven main categories includes: physical, psychological, sexual & intimate relationships, social, employment and financial, educational, and lifestyle. Further psychometric testing will be conducted to test re-test reliability, factor analysis, correlation coefficient and Cronbach's coefficient alpha. The analyses will be completed and presented at the congress.

**Conclusion:** Once the EIQ is developed and evaluated, it could be used by researchers and clinicians to measure the impact of endometriosis over time. We hope that the EIQ will provide a better understanding of the impact of endometriosis to better meet the needs of women with this condition.

**Keywords:** Endometriosis, questionnaire, validity

Friday 2 May 2014

Session - Quality of life

S7-3

**THE INFLUENCE OF DYSpareunia AND DYSmenorrhEA INTENSITIES ON DIFFERENT DOMAINS OF WOMEN'S QUALITY OF LIFE QUANTIFIED THROUGH SF-36 AND EHP-30 QUESTIONNAIRES.**

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**Objectives:** Dyspareunia and dysmenorrhoea have been the main painful symptoms related to endometriosis that impair women's quality of life (QoL). We aimed to identify domains of QoL questionnaires (SF36 and EHP30), which can be affected by dyspareunia and dysmenorrhoea in a sample of Brazilian women with deep infiltrating endometriosis.

**Design:** Cross-sectional (pre-planned) observational study (Canadian Task Force Classification II-2) including a total of 80 patients living in Rio de Janeiro (ages 19-52 years). Period: June/2011 to August/2013. Dyspareunia and dysmenorrhoea were evaluated through a visual analogue scale (VAS: 0-10). Besides, SF36 and EHP30 self-reported QoL questionnaires (Brazilian versions) were applied.

**Materials and Methods:** Assessed SF36 QoL-domains: vitality (VIT), physical-functioning (PF), bodily-pain (BPain), general-health-perception (GHP), physical-role-functioning (PRF), emotional-role-functioning (ERF), social-role-functioning (SRF) and mental-health (MH). Assessed EHP30 QoL-domains: pain, control-powerlessness (CP), social-support (SS), emotional-well-being (EWB), self-image (SI), work, sexual-relationship (SR), feelings-about-medical-profession (FAMP), about-treatment (FAT) and about-infertility (FAI); relationship-with-child/children was not assessed due to several nulliparous.

**Results:** Dysmenorrhoea and dyspareunia VAS-scores weren't statistically correlated ( $r=.020$ ;  $p=.863$ ). Concerning SF36 QoL-domains, dyspareunia showed significant correlation with (from highest to lowest Spearman's correlation coefficient): SRF ( $r=-.462$ ;  $p<.001$ ), VIT ( $r=-.444$ ;  $p<.001$ ), ERF ( $r=-.411$ ;  $p=.001$ ), MH ( $r=-.401$ ;  $p=.001$ ), PF ( $r=-.391$ ;  $p=.001$ ), PRF ( $r=-.390$ ;  $p=.001$ ), GHP ( $r=-.327$ ;  $p=.008$ ) and BPain ( $r=-.280$ ;  $p=.024$ ); dysmenorrhoea was correlated only with BPain ( $r=-.264$ ;  $p=.038$ ). Regarding EHP30 QoL-domains, dyspareunia showed the more significant correlation with SR ( $r=.528$ ;  $p<.001$ ), followed by SI ( $r=.367$ ;  $p=.003$ ), FAMP ( $r=.315$ ;  $p=.016$ ), SS ( $r=.299$ ;  $p=.016$ ) and CP ( $r=.298$ ;  $p=.016$ ); dysmenorrhoea correlated with work ( $r=.382$ ;  $p=.006$ ), pain ( $r=.333$ ;  $p=.008$ ) and CP ( $r=.320$ ;  $p=.011$ ). We proposed significant multiple linear regression models (method: enter) to evaluate tendencies of each QoL-domain as a function of dyspareunia and dysmenorrhoea (adjusted for age).

**Conclusion:** Under an exploratory viewpoint, significant tendencies were found. In resume, SF-36 QoL domains weren't influenced by dysmenorrhoea, whereas dyspareunia impaired all of QoL domains. Yet, regarding EHP-30 domains, dyspareunia influenced more domains than dysmenorrhoea (6 vs 4 domains). In conclusion, dyspareunia was the main painful symptom concerning QoL.

**Keywords:** Pain; Dyspareunia; Dysmenorrhoea.

Friday 2 May 2014

Session - Quality of life

S7-4

**AFFECTED SEXUAL FUNCTIONING IN WOMEN WITH ENDOMETRIOSIS INFLUENCES SEXUAL FUNCTIONING OF THEIR MALE PARTNER AND LEADS SUBSEQUENTLY TO UNCERTAINTY IN THEIR RELATIONSHIP**

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**Objectives:** There is a growing body of evidence indicating that dyspareunia caused by endometriosis alters women's sexual functioning. However, the extensiveness of sexual dysfunction and relation with coping strategies and quality of life and the effects on the sexual functioning of the male partner are less explored areas.

**Design:** In this cross-sectional questionnaire based study, sexual functioning of women with endometriosis (n=83) and their male partners (n= 74) was investigated. The outcomes of women were compared with a control group of women attending the outpatient department for contraception (n=41) in the period between June 2011 and December 2012.

**Materials and Methods:** We measured pain scores with the Visual Analogue Scale (VAS 0-10), sexual functioning of women with the Female Sexual Functioning Index (FSFI), quality of life with the ShortForm-12 (SF-12), pain-related thoughts with the Pain Catastrophizing Scale (PCS) and sexual functioning of men with the International Index of Erectile Function (IIEF).

**Results:** Women with endometriosis reported dyspareunia more frequently than controls (53% versus 15%, odds ratio 7.8, P<0.01) and considerably more often sexual dysfunction based on the FSFI (53% versus 11%, odds ratio 8.6, P<0.01). Sexual functioning in women with endometriosis was correlated with the VAS for dyspareunia (r=0.66, P<0.01), the SF-12 physical component (r=0.41, P<0.01) and mental component (r=0.47, P<0.01) and with all of the IIEF subscales obtained from the male partners. There was no correlation with the PCS (P=0.10) or VAS for dysmenorrhea (P=0.68). Furthermore, half of the women with endometriosis (52%) were afraid to lose their partner because of the effect of endometriosis on their sexual functioning.

**Conclusion:** Sexual dysfunction due to dyspareunia is a major concern in women with endometriosis and is correlated with lower quality of life. Remarkably pain-related thoughts do not influence sexual functioning. Affected sexual functioning of women influences sexual functioning of their male partners and leads subsequently to uncertainty in their relationship.

**Keywords:** Sexual function

Friday 2 May 2014

Session - Quality of life

S7-5

**ORAL PRESENTATION - A LONG TERM PROSPECTIVE OBSERVATIONAL STUDY OF THE IMPACT OF LAPAROSCOPIC EXCISION OF ENDOMETRIOSIS ON QUALITY OF LIFE PARAMETERS.**

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**Objectives:** The aim of this study was to demonstrate benefit in quality of life parameters and pain scores following surgery, and to determine the duration of symptom improvement, the post-operative rate of recurrence, the re-operation rate and the impact on fertility.

**Design:** This prospective observational study was carried out between January 2004 and January 2010. Ethical approval was obtained.

**Materials and Methods:** The validated quality of life instruments; SF-12, Euro QOL and the sexual activity questionnaire were used pre-operatively and post-operatively. Long term post-operative follow up varied from 2 years to over 6 years. SPSS statistical software was used for data analysis.

**Results:** Post-operative follow-up ranged from 2 years to over 6 years. Mental and physical component summary scores of the SF-12 were significantly improved in women with poorer pre-operative scores. The majority (18.5%) of women who underwent re-operation did so in the first three years of the index operation. Seventy one percent of women with sub-fertility who were desirous of a pregnancy conceived following surgery.

**Conclusion:** Laparoscopic radical excision of endometriosis significantly improves quality of life and this improvement lasts for 5 years or more. Women with a poorer quality of life scores derive the greatest benefit from surgery.

**Keywords:** Endometriosis, QOL

Friday 2 May 2014

Session - Quality of life

S7-6

**DIFFERENCES IN PAIN REPORTING AND MANAGEMENT BETWEEN THREE GEOGRAPHICAL REGIONS IN A CROSS-SECTIONAL STUDY IN PATIENTS WITH ENDOMETRIOSIS (FEELING)**

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**Objectives:** Identify factors associated with endometriosis and its grading.

**Design:** Multicenter, multi-national, cross-sectional, prospective study.

**Materials and Methods:** 720 women aged 18-41 years with histologically proven endometriosis. Data from China [390], Russia [220] and France [110] were collected.

**Results:** Reports of dysmenorrhea were fewer in Russia (55.3%) than in China (65.4%) and France (84.5%), while patients from China reported the lowest pain intensity and least impact on daily activities from dysmenorrhea. Chinese patients reported least non-cyclic chronic pelvic pain (16.4%), pain at ovulation (6.9%) and deep dyspareunia (15.4%) compared with Russia (50.2%; 42%; 52.5%) and France (50.9%; 44.5%; 58.2%). Oral contraceptive prescriptions were higher in Russia (61.4%) than in France (35.2%) and China (17.4%); while GnRH agonists were most commonly prescribed in China (53.9%) and France (50%) and lowest in Russia (29.8%). There were significantly more prescriptions of oral contraceptive pills as pain relief treatment for severe primary dysmenorrhea in France (44.1%) than in Russia (14.3%) or China (4.1%).

**Conclusion:** These results demonstrate variations in pain reporting and management for endometriosis between countries with different cultural, ethnic and socioeconomic backgrounds.

**Keywords:** Endometriosis

Friday 2 May 2014

Session - Quality of life

S7-7

**PREOPERATIVE SF36 SCORE TO DECIDE A SURGICAL APPROACH IN PATIENT WITH CHRONIC PELVIC PAIN**

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**Objectives:** To describe a new clinical tool to manage patient with chronic pelvic pain. we evaluated the benefits of preoperative SF-36 score as a predictor of improvement in quality of life after surgery in patients complaining of chronic pelvic pain and diagnosed with minimal endometriosis at laparoscopy.

**Design:** Prospective and multicenter study between February 2004 and 2011, including 652 patients with endometriosis with 168 minimal endometriosis.

**Materials and Methods:** Success was defined as an improvement of 5 points of the Physical Component Summary (PCS) or the Mental Component Summary (MCS) subscales of the SF-36 questionnaire. For Model 1, an improvement of both scores was necessary whereas for model 2, an improvement of only one of the scores was considered

**Results:** Multivariate analysis shows only two significant variables: MCS higher than 40 (OR= 4.6 for model 1 and 4.3 for model 2) and PCS higher than 50 (OR=10.6 or 3.2 for respectively model 1 and model 2). Multivariate analysis shows only two significant variables: MCS higher than 40 (OR= 4.6 for model 1 and 4.3 for model 2) and PCS higher than 50 (OR=10.6 or 3.2 for respectively model 1 and model 2). Preoperative pain score, patient age and the surgical technique used were not adequate to predict clinical post operative results.

**Conclusion:** Preoperative assessment of quality of life may be used to decide which patients complaining of chronic pelvic pain may benefit from a laparoscopic approach of the pelvis. In Patients who do not have a severe alteration of their quality of life, a laparoscopic approach may not be useful.

**Keywords:** Minimal endometriosis, pain

Saturday 3 May 2014

Seminar #9 - Endometriosis and cancer

M9-1

**CLINICAL ANALYSIS OF OVARIAN EPITHELIAL CARCINOMA WITH COEXISTING PELVIC ENDOMETRIOSIS**

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**Objectives:** To explore the differences between women with endometriosis associated ovarian cancer and typical epithelial ovarian cancer. Clinicopathological features (age at present /FIGO stage /histology/Ca125/type of dualistic model of ovarian carcinoma )were analyzed to find the association between endometriosis and ovarian cancer.

**Design:** The medical charts of total 226 patients with epithelial ovarian cancer treated at Peking Union College Hospital between 2011 and March 2012 were reviewed .Histology evaluation determined endometriosis associated ovarian cancer(n=17)or nonendometriosis associated ovarian cancer(n=209).

**Materials and Methods:** Statistical analysis for clinicoathologic variables between 2 groups was performed with chi-square or Fisher exact tests as indicated. All P values reported are 2 tailed and P value of .05 or less was considered to be statistically significant.

**Results:** Compared with nonendometriosis associated ovarian cancer, patients with endometriosis associated ovarian cancer were proved :1) to be younger and more likely to be premenopausal at diagnosis of epithelial ovarian cancer (p=0.03 and 0.005, respectively )2) to have lower preoperative serum level of Ca125(mean:122.9 vs 1377.5U/ml,P<0.001)and more likely to display normal Ca125 level(P<0.001);4)to have completely different distribution of histological subtypes (significant overrepresentation of clear cell and endometrioid carcinoma).Further more type I of EOC showed higher possibility of coexisting with endometriosis when compared with type II tumor(18.3% vs1.4%,P<0.01)

**Conclusion:** :Patients with endometriosis associated ovarian cancer differ from nonendometriosis associated ovarian cancer in many of their critical clinical and biologic characteristics. Type I of epithelial ovarian carcinoma shows higher possibility of coexisting with endometriosis.

**Keywords:** Ovarian carcinoma,epidemiology

Saturday 3 May 2014

Seminar #9 - Endometriosis and cancer

M9-2

**ENDOMETRIOSIS AND CANCER: HOW SHOULD WE LOOK TO THIS ASSOCIATION? BAF250A AND CANCER-RELATED CHEMOKINES EXPRESSION IN ENDOMETRIOSIS LESIONS AND PELVIC LYMPH NODES**

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**Objectives:** The aim of this study was to investigate in which ways endometriosis might be related to cancer: 1) endometriosis lesions progressing to cancer; 2) endometriosis lesions mimicking cancer dissemination mechanisms

**Design:** Case-control observational study Cases: 1) Evaluating BAF250a protein expression among all types of endometriosis lesions and in the pelvic sentinel lymph nodes (SLN) from patients with DIE; 2) Assessing cancer-related chemokines and their receptors (CXCL12-CXCR4; CCL19-CCR7; CCL21-CCR7) expression in DIE and respective SLN. Controls: endometrial samples from patients without endometriosis.

**Materials and Methods:** Materials: 115 women were enrolled in this study. Cases: RV-DIE (26) and their respective SLN (30), endometriomas (21), and peritoneal endometriosis (21); Controls: endometrium from patients surgically treated for benign gynecological disorders (21). Peritoneal fluid: subgroup (30 patients, 15 with and 15 without endometriosis). Methods: 1) immunohistochemistry; 2) ELISA assay

**Results:** We have only preliminary results so far. 1) The complete loss of BAF250a expression, which is related to mutations of the tumor-suppressor gene ARID1A, which in turn could lead to carcinogenic transformation, can be found in endometriosis lesions, mainly in endometriomas. We still have to look at the lymph nodes. 2) Expression of some chemokines and their receptors, especially CXCL12 (SDF-1) and CXCR4, appears to be elevated in DIE compared to normal endometrium. The correlation between the expression of the chemokines ligands and their receptors will be checked among the DIE lesions and respective SLN. Furthermore, the levels of studied chemokines seem to be higher in the peritoneal fluid from patients with endometriosis. Statistical analysis will be ready as soon as we finish all experiments.

**Conclusion:** The loss of expression of BAF250a in some endometriomas could indicate a risk of malignant transformation in such rare cases and should not be used as a prognostic marker so far. The mechanism of disease spread in endometriosis seems to be similar to cancer processes, where chemokines play especial role.

**Keywords:** Endometriosis; Cancer; Chemokines

Saturday 3 May 2014

Seminar #9 - Endometriosis and cancer

M9-3

**ENDOMETRIOSIS AND OVARIAN CANCER: AN INTERNATIONAL POOLED ANALYSIS**

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**Objectives:** Prior studies suggested that endometriosis is related to ovarian cancer, but less is known about its relationship to tumor characteristics. We undertook the largest-yet international analysis of the association between self-reported endometriosis and diagnosed ovarian cancer, allowing us to look at endometriosis and ovarian cancer histological subtype, grade, and stage.

**Design:** Pooled analysis of ovarian cancer case-control studies.

**Materials and Methods:** From the Ovarian Cancer Association Consortium, all 13 eligible case-control studies (with data on histologic subtype) were included. Logistic regression analyses were conditioned on age, ethnic origin, and study site, and adjusted for parity, and duration of oral contraceptive use. Stratified analyses were conducted by histologic subtype, grade, and stage.

**Results:** 7911 cases with invasive ovarian cancer, 1907 women with borderline ovarian cancer and 13,266 controls were included in this analysis. Endometriosis was associated with clear cell (OR 3.05, 95% CI 2.43-3.84), endometrioid (OR 2.04, 95% CI 1.67-2.48) and low-grade serous (OR 2.11, OR 1.39-3.20) ovarian cancers. No significant association was found for high-grade serous, mucinous, or borderline tumors. Among women with clear cell, low-grade serous and endometrioid invasive ovarian cancers, stage and grade were not different among women with and without endometriosis. Our results thus replicate previous findings associating endometriosis and endometrioid and clear cell ovarian cancers. They add low-grade serous tumors to the list of those putatively linked to endometriosis.

**Conclusion:** The consistency and specificity of these links suggest that endometriosis is a precursor lesion for ovarian cancer. Although most women with endometriosis will not develop ovarian cancer, limited data suggests that among affected women, ovarian cancer risk might be reduced by oophorectomy – a strategy that urgently calls for validation.

**Keywords:** Ovarian cancer, epidemiology

Saturday 3 May 2014

Seminar #9 - Endometriosis and cancer

M9-4

**MMP-3 MEDIATED ENDOMETRIOTIC SIGNALLING: GOOD OR EVIL?**

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**Objectives:** Endometriosis is believed to be a benign disease, although several study reported endometriosis may progress to invasive carcinoma, particularly in ovary. The present study aims to understand how persistent upregulation of matrix metalloproteinases (MMP) is involved in the cellular transition during endometriosis associated malignancy.

**Design:** Serum and endometriotic tissue samples were collected from different stages, based on revised ASRM guidelines for classification of endometriosis with proper consent; along with marker CA125 was recorded.

**Materials and Methods:** Zymography was used for evaluation of proteolytic activities of MMPs. For expression, Western blot was performed with human reactive antibodies. For band analysis, densitometric analysis was performed with suitable software. Statistical analysis was performed with Graphpad 3 software.

**Results:** In serum samples (n=25), exhibited gradual upregulation of proMMP-3 along with severity of the disease as judged by casein zymography. Tissues from stages III and IV disease (n=15) showed ~ 6 fold increased proMMP-3 activity. Thus, ectopic expression for proMMP-3 was very robust in comparison to expression in systemic fluid, like in serum. In addition, proMMP-2 activity in serum samples (n=25) was moderate while that is high in respective tissue samples. Furthermore, in eutopic tissues (n=10), women with endometriosis had significantly higher proMMP-9 and -2 activity than women without endometriosis. Eight women under stage III-IV of endometriosis were diagnosed with increased CA-125, which corroborated to our finding of increased proMMP-3 activity, along with MMP-7 activity in biopsy samples.

**Conclusion:** As MMP-3 is involved in epithelial to mesenchymal transition (EMT), herein, endometriosis-associated malignancy might result from increased MMP-3 activity and warrants further studies on TGF- $\beta$  mediated signaling pathways.

**Keywords:** Endometriosis, MMPs, Malignancy

Saturday 3 May 2014

Seminar #9 - Endometriosis and cancer

M9-5

**OVARIAN CANCER AND ENDOMETRIOSIS – SHARING ALTERED GENETIC PATHWAYS?**

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**Objectives:** To find similar genetic pathways in ovarian endometriosis and cancer that can explain malign transition from ovarian endometriotic implants.

**Design:** Searching in the literature for commonly deregulated expressed genes in both ovarian endometriotic lesions and different types of cancer.

**Materials and Methods:** We selected a roll of genes in articles that had screened differential gene expression between endometriotic lesions (which included ovarian lesions) and normal endometrial tissue of women without endometriosis. We searched articles in PUBMED site combining the official symbol of each deregulated gene in endometriosis with the keyword “cancer”.

**Results:** after the analysis of almost 1100 published studies, we found that from more than 140 different expressed genes in endometriosis (previously registered in the literature) approximately 17% are also deregulated in ovarian cancer, including AXL, JUND and FOSB. The genes are involved in many cellular functions that are important for endometriosis and cancer onset and development, like growth, migration, aggregation, apoptosis, differentiation and transformation.

**Conclusion:** The results may drive, hereafter, appropriated diagnostics and treatments in cases of ovarian endometriosis malignization as well as bring new insights about the origin and development of endometriosis. Despite of this new informative data, future studies of our group will be done to confirm the results of the present work.

**Keywords:** Cancer, Endometriosis, Genes

Saturday 3 May 2014

Seminar #10 - Prevention and management of recurrences

M10-1

**ENDOMETRIOSIS: AN INTERNATIONAL HEALTH ISSUE TOO BIG TO IGNORE - PREVENTIVE PROGRAMS INTEGRAL TO A MULTI-DISCIPLINARY APPROACH TO TREATMENT, A NEW ZEALAND MODEL.**

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**Objectives:** To determine whether an integrated, professional approach by an endometriosis organisation can be pivotal in providing specialised, pragmatic, preventive solutions to the burdens caused by endometriosis through a whole community approach to raise awareness, encourage early intervention, address unacceptable statistics and improve health outcomes for women and girls with endometriosis.

**Design:** Endometriosis New Zealand (Registered Charitable Trust founded in 1985), has initiated programs for schools (Menstrual Health and Endometriosis secondary school program titled 'me'), hospitals, workplaces and communities. Programs support empirical research on diagnostic delay, the impact on quality of life and fertility with literature confirming clinical, societal and financial burdens.

**Materials and Methods:** The method uses this evidence, insights, intuition and innovation to initiate, structure, resource and deliver each program using strengths based and well-health programs for schools, workplaces, hospitals and communities. Program evaluation uses mixed methodology: survey evaluations, in addition to observational study data generated from focus groups, feedback and peer review.

**Results:** A novel data set from uniquely structured programs will be presented. 'me' program data show; 30% usually/always experience painful periods, 18% have school absenteeism and 28% report lifestyle interferences. Private clinic results over a 10 year period, show a five-fold increase in presentation of symptoms suspicious of endometriosis in women under 20. The Public Hospital Patient Partnering Program showed an overall self-reported quality of life improvement, fulfilling patients' needs to be understood, to understand, and be integral in their health-care. Synopses of workplace programs, seminars and the 2013 initiative 'dance-for-me' will be presented. Surgical intervention based on incidence of endometriosis estimate that New Zealand gynaecological surgeons, need 10-hour operating lists, 7 days/week, 48 weeks/annum to meet demand, but most gynaecologists have 4-8 hours operating time/week.

**Conclusion:** The international scale of endometriosis is insurmountable by best practice surgery alone. A multi-disciplinary approach can now conceivably incorporate well-health, best practice professional programs with a whole community approach to early intervention and prevention, integrating into appropriate management and best practice treatment.

**Keywords:** Prevention, well-health, multi-disciplinary

Saturday 3 May 2014

Seminar #10 - Prevention and management of recurrences

M10-2

**OCCULT ENDOMETRIOSIS: AN UNDETECTABLE FINDING BY LAPAROSCOPY IN NORMAL PERITONEUM**

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**Objectives:** Laparoscopy is a gold standard modality to detect/treat visible endometriosis. Even with the careful eyes of expert surgeons, there is obvious chance to miss occult lesions in visually normal peritoneum. Here we investigated a decade old concept of invisible (occult) microscopic endometriosis in women with and without visible endometriosis.

**Design:** This is a case-controlled biological research using prospectively collected visually normal peritoneal samples from different anatomical sites of pelvis from 151 women with visible endometriosis and 52 control women during laparoscopy and their retrospective histological evaluation.

**Materials and Methods:** A histological search of all peritoneal biopsy specimens for the detection of occult endometriosis (OE) was done and confirmed by immunoreaction to Ber-EP4 (epithelial cell marker), CD10 (stromal cell marker), and Calretinin (mesothelial cell marker). Tissue expressions of estrogen/progesterone receptors (ER/PR) and cell proliferation marker, Ki-67 were performed by immunohistochemistry.

**Results:** Three different patterns of OE were detected based on (I) presence of typical gland/stroma, (II) reactive hyperplastic change of endometrioid epithelial cells with surrounding stroma, and (III) single-layered epithelium-lined cystic lesions with surrounding stroma. A higher tendency in the occurrence of OE was found in women with visible endometriosis (15.2%, 23/151) comparing to control women (6.4%, 4/62) ( $p=0.06$ , X<sup>2</sup> test). The epithelial cells and/or stromal cells of OE lesions were immunoreactive to Ber-EP4/CD10 but non-reactive to Calretinin. Variable ER and PR expression was observed in all patterns of OE lesions. Ki-67 index (percentage of Ki-67-positive nuclei among total cells) was significantly higher in pattern I/II OE lesions than in pattern III OE lesions ( $p<0.05$  for each).

**Conclusion:** We re-confirmed a decade long old concept of invisible (occult) endometriosis in visually normal peritoneum of women with visible endometriosis. Although rejected by previous reports, we found that a proportion of these occult peritoneal lesions displayed a variable amount of tissue activity.

**Keywords:** occult endometriosis, Ki-67

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Seminar #10 - Prevention and management of recurrences

M10-3

ENDOMETRIOTIC LESIONS RECAPITULATE WOUND HEALING BY RECRUITING PLATELETS

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**Objectives:** One hallmark of endometriotic foci is cyclic bleeding. Yet bleeding is a cardinal hallmark of a wound. This study sought to investigate the roles of platelets in the development of endometriosis and explore ways to treat endometriosis through intervention of the platelet activation pathways.

**Design:** Cross-sectional clinical studies of women with and without endometriosis, and animal studies using P-selectin knockout and wild-type mice.

**Materials and Methods:** Immunohistochemistry analysis of ectopic/eutopic endometrial tissues from women with and without endometriosis; gene expression and protein analysis using primary cell culture. Mouse experiments were conducted to examine the effect of platelet depletion/infusion and the therapeutic efficacy of a recombinant P-selectin protein to treat endometriosis in mice with induced endometriosis.

**Results:** There was a significantly increased platelet aggregation in endometriotic lesions, concomitant with elevated VEGF expression and microvessel density. Co-culture of endometriotic stromal cells with platelets increased the expression of COX-2, MMP-9, VEGF, and Bcl-2. IL-1 $\beta$ -induced COX-2 upregulation increased production of the coagulant TXA<sub>2</sub> in endometriotic stromal cells. We not only confirmed that tissue factor (TF) expression is elevated in endometriosis but also found that the TF concentration in the supernatant of cultured primary endometriotic stromal cells and in the peritoneal fluid from women with endometriosis were both significantly elevated. Ozagrel treatment resulted in significantly reduced lesion size and improved hyperalgesia in mice with induced endometriosis, so did platelet depletion. Administration of P-selectin-Fc remarkably efficacious in treating mice with induced endometriosis.

**Conclusion:** Endometriotic lesions recapitulate wound healing mechanisms to their advantage by recruiting platelets. Viewing from this perspective, many seemingly unrelated molecular findings that are otherwise difficult to explain can be pieced together very neatly. It also points out new directions for development of novel therapeutics as well as biomarkers for endometriosis.

**Keywords:** Endometriosis, platelet, P-selectin

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Seminar #10 - Prevention and management of recurrences

M10-4

**THE ASSOCIATION BETWEEN SYMPTOMS AND SURGICAL FINDINGS IN WOMEN WITH SUSPECTED ENDOMETRIOSIS**

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**Objectives:** To determine whether there is an association between specific symptoms and surgical findings in women with suspected endometriosis.

**Design:** Multi-centre prospective observational study undertaken from January 2009 to February 2013. All women included in this study were of reproductive age, had a history of chronic pelvic pain and/or endometriosis, and had a plan for laparoscopic endometriosis surgery.

**Materials and Methods:** A detailed history was obtained and the following surgical features were recorded during laparoscopy: deep infiltrating endometriotic (DIE) nodules involving anterior rectum, rectosigmoid, uterosacral ligaments (USL), rectovaginal septum (RVS) and/or vagina. The association between surgical findings and symptoms recorded during the history were analyzed for significance using Fisher's exact test.

**Results:** The following symptoms were significantly associated ( $p < 0.01$ ) with the respective surgical findings: dyschezia – presence of any posterior compartment DIE, bowel surgery, left ovarian endometrioma; rectal bleeding - presence of any posterior compartment DIE, rectosigmoid DIE, bowel surgery, left and right ovarian fixation, and right ovarian endometrioma; tenesmus - presence of any posterior compartment DIE, right ovarian fixation; left iliac fossa pain – left and right ovarian fixation; right iliac fossa pain- rectovaginal septum DIE.

**Conclusion:** This study showed that women with dyschezia, rectal bleeding and/or tenesmus are at increased risk of having posterior compartment DIE and should therefore undergo a detailed pre-operative TVS assessment for the mapping of possible posterior compartment DIE prior to surgery.

**Keywords:** Endometriosis, symptoms, laparoscopy

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Seminar #10 - Prevention and management of recurrences

M10-5

**ANTI-ANGIOGENESIS OF GREEN TEA AND POTENTIALS OF PRODRUG OF EPIGALLOCATCHIN-3-GALLATE (PRO-EGCG) AS A NOVEL ANTI-ANGIOGENESIS AGENT FOR ENDOMETRIOSIS**

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**Objectives:** There is urgent need in seeking better therapeutic approaches for endometriosis. Anti-angiogenesis therapy offers a new opportunity. Small anti-angiogenic molecules derived from natural products have great potential and advantages over synthetic inhibitors. We compared the anti-angiogenesis of green tea polyphenols and evaluated efficacy and safety of its prodrug for endometriosis.

**Design:** In vitro and in vivo angiogenesis assays for endometriosis.

**Materials and Methods:** Established in vitro endothelial cell culture tests, in vivo modified Miles vascular permeability assay and in vivo experimental endometriosis models were employed to characterize the anti-angiogenic potentials of green tea extract for endometriosis and to compare the anti-angiogenic effects of green tea polyphenols and prodrug on endometriosis.

**Results:** EGCG and prodrug has more potent antioxidant-independent inhibitory effects on the endothelial proliferation, migration, invasion and tube formation in vitro; and also significantly inhibited the growth of endometrial implants. Prodrug significantly reduced lesion size and weight, inhibited functional and structural microvessels in the lesions, and enhanced lesion apoptosis. The inhibition by prodrug in all the angiogenesis parameters was significantly greater than that by EGCG, with better bioavailability and greater anti-oxidation and anti-angiogenesis capacities than EGCG. Ovarian follicles and uterine endometrial glands were not affected by either EGCG or prodrug. Oral administration of prodrug has same efficacy for endometriosis.

**Conclusion:** Green tea EGCG and Prodrug significantly inhibited the development, growth and angiogenesis of experimental endometriosis in mice with high efficacy, bioavailability, anti-oxidation and anti-angiogenesis capacities. Prodrug could be a potent anti-angiogenesis agent for endometriosis.

**Keywords:** Endometriosis, Angiogenesis, GreenTea

Saturday 3 May 2014  
Session - Endometrium

S8-1

**RATIONAL DESIGN OF SYNTHETIC EXTRACELLULAR MATRIX (ECM) MICROENVIRONMENTS THAT FOSTER ENDOMETRIAL EPITHELIAL CELL POLARITY, FUNCTION, AND STROMAL CROSSTALK FOR IN VITRO AND IN VIVO USE**

Christi Cook<sup>1</sup>, Michael Beste<sup>1</sup>, Emily Prentice<sup>1</sup>, Nurşen Öğütveren<sup>1</sup>, Keith Isaacson<sup>2</sup>, Linda Griffith<sup>1</sup>

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**Objectives:** Our objective is to dramatically improve the ease, reproducibility, and functionality of 3D endometrial cultures for use in mechanistic studies of endometriosis by developing an entirely synthetic extracellular matrix (ECM) that recapitulates the desirable features of natural basement membrane (Matrigel) in fostering polarized endometrial luminal and glandular epithelial behaviors.

**Design:** A semi-empirical approach was used to design and screen a panel of polyethylene glycol (PEG)-based hydrogels incorporating cell adhesion moieties and proteolytic degradation sites. Features were chosen to foster cell attachment, polarization, and stabilization of cell-secreted basement membrane by Ishikawa cells and primary cells isolated from endometrial biopsies.

**Materials and Methods:** Luminal and glandular endometrial epithelial tissue culture models were developed using Michael-type chemistry multiarm-PEG hydrogels with matrix metalloproteinase degradable crosslinks functionalized with an assembled peptide library of biomimetic extracellular matrix ligands from basement membrane proteins. Epithelial cell attachment, polarity and barrier functionality were assessed by immunofluorescence of apical/basal protein localization.

**Results:** A fully synthetic PEG matrix was engineered to support a two-dimensional polarized luminal epithelium and adapted to support a three-dimensional glandular spheroid model. Through a morphogenesis screen using >50 PEG hydrogels with individual or combinations individual peptide ligands derived from basement membrane ECM or a stabilizer of ECM, formulations were identified that fostered Ishikawa and primary epithelial attachment and epithelial polarization (apical actin localization) to a degree comparable to a reconstituted basement membrane preparation, Matrigel. An optimal hydrogel formulation was identified that recapitulated epithelial basement membrane features through incorporation of matrix metalloproteinase 1 proteolytically degradable crosslinks for cell-mediated remodeling, engagement of cell adhesion receptors for attachment, and capture of cell-secreted laminin that fostered enhanced polarization for the support of robust epithelial culture models.

**Conclusion:** The design of highly defined tissue culture models enables the study of signaling events that mediate epithelial cell survival, attachment, and invasion processes relevant to endometriosis pathophysiology. We establish a fully synthetic tissue culture scaffold to support robust, highly reproducible luminal and glandular endometrial models of polarized epithelial cells.

**Keywords:** Endometrium, Epithelium, Extracellular-matrix

**Saturday 3 May 2014**  
**Session - Endometrium**

**S8-2**

**ALTERED MOLECULAR PHENOTYPES OF EUTOPIC ENDOMETRIAL MESENCHYMAL STEM CELLS AND STROMAL FIBROBLASTS IN ENDOMETRIOSIS**

Juan Irwin<sup>1</sup>, Fatima Barragan<sup>1</sup>, Terhi Piltonen<sup>2</sup>, Trimble Spitzer<sup>1</sup>, David Erikson<sup>1</sup>, Linda Giudice<sup>1</sup>

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**Objectives:** Eutopic endometrial tissue and cultured endometrial stromal fibroblasts of women with endometriosis display altered gene expression compared to controls. Herein we investigated whether endometrial stromal fibroblasts (eSF) and their putative progenitors, the endometrial mesenchymal stem cells (eMSC), have altered molecular phenotypes in women with endometriosis in vivo.

**Design:** Global expression profiling of cell populations isolated by fluorescence-activated cell sorting (FACS) from proliferative phase eutopic endometrium of women with endometriosis (n=5: 1 minimal, 1 mild, 3 severe) and from controls without endometriosis (n=5).

**Materials and Methods:** Proliferative phase endometrial tissue samples were obtained from biopsy or hysterectomy specimens through the NIH-SCIPPR Human Endometrial Tissue Bank at UCSF, enzymatically dissociated, and CD146+/PDGFRB+ (eMSC) and CD146-/PDGFRB+ (eSF) populations isolated by FACS. RNA from sorted cells was analyzed on Affymetrix 2.0 ST expression arrays with data bioinformatics using GeneSpring.

**Results:** By hierarchical clustering, eMSC and eSF transcriptomes clustered primarily by cell type, then by disease. A common set of 3,794 differentially expressed genes distinguished eMSC and eSF in both endometriosis and controls. Comparison of corresponding cell populations in endometriosis vs. controls revealed differential expression (>1.5-fold) of 387 genes in eSF, and 289 genes in eMSC. Upregulated eSF genes in endometriosis included CXCL2, CD83, CXCL2, DIO2, IL8, TNC, MMPs, the latter three implicated in endometriosis pathogenesis. Downregulated eSF genes in endometriosis included TYMS, DHFR, CDK1, cyclins, kinesins. Upregulated eMSC genes in endometriosis included TNC, DIO2, MMPs, PDGFRA, MME, LOX, WNT5A, ALDH1A1, the latter five normally upregulated in eSF vs. eMSC. Downregulated eMSC genes in endometriosis included TYMS, DHFR, CDK1, cyclin B, and kinesin 15.

**Conclusion:** Eutopic eSF have an aberrant molecular phenotype in endometriosis, potentially relevant to pathogenesis, and suggestive of eSF functional dyssynchrony in endometriosis during proliferative phase. eMSC transcriptome changes in endometriosis included upregulation of eSF-associated genes, and raised the possibility of a disease eSF phenotype inherited from eMSC progenitors.

**Keywords:** Endometriosis, endometrial-mesenchymal-stem-cells, endometrial-stromal-fibroblasts

**Saturday 3 May 2014**  
**Session - Endometrium**

**S8-3**

**THE ORIGINS OF PROGESTERONE RESISTANCE IN ENDOMETRIOSIS: SILENCING OF PROGESTERONE ACTION AT MENSTRUATION**

Bruce Lessey<sup>1</sup>, Warren Nothnick<sup>2</sup>, Asgerally Fazleabas<sup>3</sup>, Niraj Joshi<sup>3</sup>, Steven Young<sup>4</sup>

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**Objectives:** Objective: Endometriosis is a disease characterized by progesterone (P) resistance. The origin of P resistance is unknown but likely related to inflammation. The object of this study was to investigate the hypothesis that P resistance is a natural mechanism of menstruation that curtails P actions and is co-opted by endometriosis.

**Design:** Laboratory research on normal endometrial tissues.

**Materials and Methods:** RNA was extracted from each endometrial biopsy and analyzed by quantitative RT-PCR for microRNA (miR)-29c. FKBP4 (aka FKBP52), a progesterone receptor chaperone protein target of miR-29c. Data were analyzed by one-way ANOVA followed by Tukey-Kramer post-hoc analysis.

**Results:** Compared to early secretory (ES) and mid-secretory (MS) endometrium, miRNA29c expression was significantly higher in late secretory (LS)/menstrual endometrium (P=0.0158). In these samples, FKBP4 was suppressed in the LS/premenstrual samples compared to ES and MS. We previously demonstrated elevated miR-29c in the endometrium during the MS phase in baboons with endometriosis and this was correlated with reduced FKBP4 expression. This expression pattern was further correlated with the ultrastructural morphology which was representative of a LS endometrium as opposed to a MS endometrium. These results suggest that P-resistance seen in endometriosis is comparable to changes observed as part of the events leading to menstruation which is also characterized by a decrease in P support.

**Conclusion:** We present a mechanism during early menstruation whereby P-action is actively curtailed. Blockade of P is likely to be part of an inflammatory cascade that occurs at menses but is prematurely elicited in the endometrium of women with endometriosis, resulting in infertility and endometrial changes that contribute to its pathophysiology.

**Keywords:** Progesterone, endometrium, endometriosis.

**Saturday 3 May 2014**  
**Session - Endometrium**

**S8-4**

**MICRORNA MIR-142-3P REGULATES PROINFLAMMATORY SIGNALING IN ENDOMETRIAL STROMA CELLS**

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**Objectives:** microRNAs, noncoding RNAs implicated in regulating gene expression posttranscriptionally, are dysregulated in endometriosis. Here, we investigate the role of one dysregulated miRNA, miR-142-3p, in proinflammatory signaling in endometrial stroma cells.

**Design:** Experimental in vitro study on the immortalized endometrial stroma cell line ST-T1 and primary endometrial stroma cells from endometriosis patients.

**Materials and Methods:** ST-T1 cells and primary endometrial stroma cells were transiently transfected with miR-142-3p precursors or control reagents. The impact of miR-142-3p expression on predicted target gene expression was monitored by qPCR. Signal transduction analysis was performed by Western blotting following stimulation with IL-6. Cell viability was investigated by MTT assay.

**Results:** Upregulation of miR-142-3p significantly reduced expression of the IL-6 coreceptor IL6ST. Cell viability was moderately, yet reproducibly affected, resulting in a 10% reduction upon miR-142-3p transfection.

Downregulation of IL6ST was associated with a significantly reduced activation of STAT3 upon IL-6 stimulation in vitro, and with a change in basal expression levels of the inflammatory master regulator NFkB.

**Conclusion:** miR-142-3p is a novel regulator of IL-6 dependent signalling in endometrial stroma cells. Dysregulated expression of miR-142-3p in endometriosis may therefore contribute to the pathogenetic mechanism via modulation of inflammatory processes.

**Keywords:** microRNA, inflammation, IL-6

**Saturday 3 May 2014**  
**Session - Endometrium**

**S8-5**

**DECREASE IN NOTCH 1 CONTRIBUTES TO IMPAIRED DECIDUALIZATION ASSOCIATED WITH ENDOMETRIOSIS.**

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**Objectives:** To determine if the decrease in Notch 1 receptor and ligand expression, a universal arbiter of cell fate, which is critical for the initiation of decidualization in primates and rodents, contributes to the blunted decidualization response in stromal fibroblasts isolated from the eutopic endometrium (EuE) of women with endometriosis.

**Design:** Whole EuE tissues (n=7-10) and stromal fibroblasts for the in vitro decidualization experiments in the presence of estrogen, progesterone and cAMP (n=4) were obtained from women with and without disease. For shRNA and microarray experiments human uterine fibroblasts (HuF) cells were utilized from disease free women (n=3-4).

**Materials and Methods:** EuE sections and RNA were analyzed for Notch receptors, Notch ligands and target gene expression by IHC and qRT-PCR. Stromal fibroblasts were decidualized in vitro for 8d. HuF cell were transfected with Notch 1 shRNA or scrambled control for 3d and incubated in decidualization media for 6d.

**Results:** Notch receptors (1&4), ligands (Jag2 & Dll4) and targets Hes5 & Hey1 were significantly downregulated (p<.01) in EuE of women with endometriosis. Following decidualization the same genes together with decidualization markers IGFBP1 and Prl were also decreased (p<.01) in EuE endometriotic fibroblasts. Silencing of Notch 1 expression in HuF cells prior to the induction of decidualization inhibited the response but silencing 5d following the initiation of treatment had no effect suggesting Notch1 is critical for the initiation of decidualization. Microarray analysis revealed that 39 genes are specifically inhibited by Notch 1 silencing during decidualization. In addition to IGFBP1, SOCS2, Complement C3, IL 15, CXCL 12 which we had previously validated in endometriotic tissues were significantly downregulated when Notch1 was silenced prior to decidualization.

**Conclusion:** The downregulation of Notch receptors and their ligands in EuE and stromal cells from women with endometriosis suggests that Notch plays a central role in the blunted decidualization associated with the disease. The decrease in Notch expression results in the suppression of immunomodulatory genes which may contribute to infertility.

**Keywords:** Notch, decidualization, endometriosis

**Saturday 3 May 2014**  
**Session - Endometrium**

**S8-6**

**PROTEIN OXIDATION LEVELS AND SUPEROXIDE DISMUTASE ACTIVITY IN WOMEN WITH INFERTILITY RELATED TO ENDOMETRIOSIS**

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**Objectives:** To evaluate role of the oxidative stress in plasma and eutopic endometrial tissue in woman with infertility related to endometriosis.

**Design:** Descriptive double-blind study between gynecological and biochemistry areas.

**Materials and Methods:** Population: twenty-two women with infertility related to endometriosis and sixteen without endometriosis. Levels of protein carbonyl and activity superoxide dismutase (SOD) in plasma and endometrial tissue samples were measured. Data were analyzed by U-Mann-Whitney test for nonparametric data. The ji-x test was used to compare isoforms of SOD.

**Results:** Significantly higher levels of carbonyl protein were observed in woman with infertility related to endometriosis compared with control group, ( $46,09 \pm 65,43$  ng carbonyl protein /  $\mu\text{g}$  total protein vs  $10,84 \pm 4,54$  ng Carbonyl protein /  $\mu\text{g}$  total protein,  $P=0,0007$ ). However, no significant differences were found in plasma samples ( $P=0,1099$ ). The presence of activity isoforms Cu/Zn and Mn superoxide dismutase was found to be significantly different in both groups ( $P=0,0031$ ). Activity isoforms Cu/Zn and Mn superoxide dismutase in women nulliparas of the both groups was compared, showing that nulliparas women with infertility related to endometriosis had activity both isoform SOD, however in those with infertility no related to endometriosis only had presence of the isoform Mn SOD.

**Conclusion:** Better understanding of the mechanisms whereby the stress oxidative and antioxidant system can influence on the eutopic endometrial tissue environment are essential to obtain new insight into this disease and eventually develop new diagnostic and therapeutics strategies.

**Keywords:** Stress, endometriosis, infertility.

Saturday 3 May 2014  
Session - Endometrium

S8-7

**DETECTION OF NERVE FIBERS IN ENDOMETRIUM TOPIC TO AID IN THE DIAGNOSIS OF ENDOMETRIOSIS**

Miguel Gobbi Neto<sup>1</sup>, Bruno Nogueira Bonilha<sup>1</sup>, Victor Arias<sup>1</sup>, Mariana Cunha De Ávila Camargo<sup>1</sup>, Larissa Codo Dias<sup>1</sup>, Rafael Reis Pereira<sup>2</sup>

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**Objectives:** Confirm the presence of cytological and functional changes in the nerve fibers of the basal and functional layer of abnormal endometrium topic of women with endometriosis by conventional endometrium biopsy, capable of providing sufficient sensitivity and specificity to suggest pelvic endometriosis.

**Design:** Setting the value of a precursor diagnostic method for early diagnosis of endometriosis minimally invasive and which could be an outpatient basis by confirming, by means of immunohistochemistry, the presence of nerve fibers of the type A-Delta and C in the endometrium topical obtained from Brazilian women with suspected endometriosis.

**Materials and Methods:** Biopsy of 30 women undergoing laparoscopy evaluated by immunohistochemistry for the presence of nerve fibers type A-delta and C During surgery were evaluated for the diagnosis of endometriosis. The Samples of endometrium immunohistochemistry were performed during the same procedure. Data were statistically analyzed using SPSS.

**Results:** Functional endometrial nerve fibers (FNF) were identified in 07 biopsies (25.8%) of the total of 27 biopsies satisfactory. Accordingly, 13 (48%) patients had laparoscopic confirmation of endometriosis and only 01 (3.6%) showed nerve fibers biopsy that was not found in endometriosis by laparoscopy. In this case, the patient was medicated with two ampoules previously GnRH analogue of 10.6 mg. Pain was the most common symptom in cases of endometriosis confirmed by laparoscopy and there was no correlation between the presence of nerve fibers and hormone therapy.

**Conclusion:** In this work, the presence of nerve fibers in endometrium topic, gathered through conventional biopsy and evaluated by immunohistochemistry showed a test with sufficient sensitivity to collaborate in the diagnosis of pelvic endometriosis, but with little specificity.

**Keywords:** fibers Immunohistochemistry Endometriosis.

**Saturday 3 May 2014**  
**Session - Epidemiology**

S9-1

**ENDOMETRIOSIS RELATED QUALITY OF LIFE OUTCOMES ARE HIGHLY INFLUENCED BY RECRUITMENT STRATEGIES**

Aisha De Graaff<sup>1</sup>, Carmen Dirksen<sup>2</sup>, Steven Simoens<sup>3</sup>, Bianca De Bie<sup>4</sup>, Thomas D'Hooghe<sup>5</sup>, Gerard Dunselman<sup>6</sup>

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**Objectives:** Most studies on quality of life in women with endometriosis are conducted in tertiary care centres or in patient associations. It is conceivable that the setting in which patient recruitment is performed influences the obtained outcome. Therefore we compared study results of women recruited in three different settings.

**Design:** Retrospective questionnaire based cohort study (part of the WERF EndoCost study). The investigated women were recruited in three different settings: a tertiary care centre for endometriosis (n=126), five secondary care centres (n=56) and an endometriosis patient association (n=276) (case mix of women treated in secondary or tertiary care).

**Materials and Methods:** Questionnaires included medical history, current symptoms, effect on daily life and quality of life expressed by the norm based scores for the physical (PCS) and mental (MCS) component of the SF-36v2. Categorical and ordinal data were compared by the Chi-square test and continuous data through the analysis of variance (ANOVA).

**Results:** More women recruited from tertiary care (67%) underwent laparotomy(s) than those recruited from secondary care (49%) and the patient association (48%)(P=0.001). Affected job was more prevalent in patient association members and tertiary care (63% and 56%) than those from secondary care (32%) (P<0.001). This was also true for affected relationships (55% and 39% versus 18%) (P<0.001). Dyspareunia was more prevalent in the patient association (56%) than in both secondary (38%) and tertiary care (49%) (P=0.01). Chronic pain was comparable between tertiary care (63%) and patient association (69%) while lower in the secondary care (45%) (P=0.005). Substantial differences in quality of life were detected between secondary care (PCS 50.6, MCS 47.2), tertiary care (PCS 45.1, MCS 44.2) and patient association (PCS 43.6, MCS 42.3) (P=<0.001, P=0.018).

**Conclusion:** Our study shows that outcomes are highly influenced by recruitment strategy. None of the groups appeared to be representative of the total population of women with endometriosis. Therefore future study populations should preferably consist of a weighted sample of both secondary and tertiary care patients.

**Keywords:** Recruitment bias, quality-of-life

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S9-2

**SMOKING EFFECTS ON PAIN SYMPTOMS AND FERTILITY IN PATIENTS WITH ENDOMETRIOSIS**

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**Objectives:** We aimed to evaluate the potential effects of smoking history as an aggravating factor for pain symptoms and infertility and its impact on gynecological and obstetric history and laboratorial markers in patients with endometriosis.

**Design:** We undertook a cohort study with ninety-three subjects formally diagnosed with endometriosis through at least one previous video-laparoscopic procedure. Subjects were subdivided by absence or presence of smoking history and were evaluated in the Gynecology Unit of Hospital de Clínicas de Porto Alegre.

**Materials and Methods:** Subjects underwent a standard protocol including clinical (presence, grade at visual analogous scale and impact on social and work life of pain symptoms; presence and time of infertility), anthropometric and laboratorial evaluation (serum CA-125 and prolactin). Chi-square test, independent-samples t-test, Mann-Whitney test and Pearson's correlation coefficient were used as appropriate.

**Results:** The study group comprised 93 subjects, of whom 29 (31.2%) had a smoking history. The mean smoking time was 11.7 years (SD ± 6.0). There was no difference between the groups at baseline characteristics and family history for endometriosis. The two groups did not differ by presence, impact or grade of pain symptoms, presence or time of infertility, gynecological and obstetric history and prolactin levels. Non-smokers had significantly higher levels of CA-125 (median of 14 U/ml vs. 10 U/ml of smokers; P = 0.006). Time of smoking did not correlate significantly with an increase in grade of pain symptoms, time of infertility and serum levels of CA-125 or prolactin.

**Conclusion:** Our findings suggest that smoking history is not important for the presence or intensity of endometriosis characteristics symptoms. Smokers had lower levels of CA-125, a laboratorial marker of endometriosis, in agreement with studies that demonstrated decreased prevalence of endometriosis and endometrial cancer in smokers.

**Keywords:** Smoking, pain, infertility

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S9-3

**INCIDENCE AND COST OF SURGERY FOR ENDOMETRIOSIS IN CANADA IDENTIFIED USING A NATIONAL DATABASE**

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**Objectives:** To provide a current estimate of the annual incidence of women requiring surgery for endometriosis and the hospital related costs associated with surgery for endometriosis in Canada.

**Design:** In this population-based cross-sectional study, women aged 18-59 with a most responsible diagnosis of endometriosis based on International Classification of Diseases (ICD-10CA) who had surgery for endometriosis with a discharge date between April 1, 2012 and March 31, 2013 were identified using the Canadian Institutes for Health Information (CIHI) Portal.

**Materials and Methods:** Surgical interventions for endometriosis were categorized as laparoscopy, adnexal surgery, hysterectomy, or other. Clinical categorisation of cases and interventions, geographical location, and relative intensity weighting (RIW) were extracted from the CIHI Discharge Abstract Database. A standard costing methodology using cost per weighted case (CPWC) was used to determine costs.

**Results:** In 2012, 2,430 women with a major diagnosis of endometriosis were admitted to an acute care hospital in Canada. The national incidence of admissions was 0.305 per 1000 female age-adjusted population, but varied between 0.244 to 0.968 depending on the Province. Of these, 1511 (62%) had hysterectomy, 467(19.2%) had adnexal surgery, 131(5.4%) underwent laparoscopy for diagnosis or treatment, and 304(12.5%) were admitted for other treatments which included bowel resection, appendectomy, and excision of soft tissue endometriosis. Peak incidence for admissions were in the age group 40-44. Hospital-related costs were \$6,875,574 for hysterectomy, \$1,908,269 for adnexal surgery, \$478,166 for laparoscopic diagnosis or treatment, and \$1,217,306 for other treatments. The total annual cost of endometriosis-related in-patient surgery in Canada was calculated to be \$10,561,075.

**Conclusion:** There are geographic variations in admission rates for endometriosis across Provinces. The most common reason for hospital admission is hysterectomy. There is a substantial economic impact from treatment of endometriosis in Canada. These results can be regarded as reliable as they are derived from an official national database.

**Keywords:** Endometriosis, cost, surgery

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**S9-4**

**ENDOMETRIOSIS HEALTH CARE: DISPARITIES IN ACCESS TO CARE IN WOMEN FROM PUERTO RICO.**

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**Objectives:** The aims of this study were: i) to examine differences between the private and public (government-based) health insurance sectors in women with endometriosis, and ii) to assess the frequency of endometriosis-related utilization services from a Health Insurance Company (HIC) in Puerto Rico.

**Design:** We conducted a transversal study of a secondary database from a major health insurance company in the Island. A total of 8,280 claims of endometriosis as a primary diagnosis (ICD-9: 617.0 to 617.9), from 2004 to 2009 were analyzed.

**Materials and Methods:** A bivariate analysis was performed to examine differences between women with endometriosis with insurance from the public and private sectors. Pearson chi-square test was used to determine significance of the differences between groups, including lesion sites, hospitalizations, emergency room visits, and place of services.

**Results:** Women with endometriosis had a mean age of  $32 \pm 7.87$  (range: 14-55y/o). Half of the patients from the private sector lived in the Metro area (55.1%), and their claims were more related to medical visits (38.0%). In contrast, most patients from the public sector lived in the South area (36.6%), and their claims were more related to laboratory tests (32.9%). Inflammatory-related diseases (28.6%) were highly prevalent in both groups. Patients with private HIC had more claims related to hospitalizations than the public sector ( $p < 0.001$ ). Patients with a private HIC were less likely to have visits to an ER ( $p = 0.004$ ). Also, there was a statistically significant difference in endometriosis lesion types between HIC sectors ( $p < 0.001$ ).

**Conclusion:** This study identified disparities in health care access in women with endometriosis in Puerto Rico. Patients with private HIC appear to have more access to health care than those from public sector. Public health programs are needed to promote access to health care for endometriosis patients irrespective from socioeconomic status.

**Keywords:** Endometriosis, Disparity, Insurance

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S9-5

**PELVIC INFLAMMATORY DISEASE IN WOMEN WITH ENDOMETRIOSIS IS MORE SEVERE THAN IN THOSE WITHOUT**

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**Objectives:** To determine the incidence and severity of pelvic inflammatory disease (PID) or tubo-ovarian abscess (TOA) in hospitalized patients with and without a history of endometriosis.

**Design:** Retrospective analysis of hospital records

**Materials and Methods:** Retrospective analysis of hospital records retrieved for all women hospitalized with PID or TOA between January 2008 and December 2011 in a tertiary referral center. Women were compared with regards to a history of endometriosis for demographic, clinical and fertility data.

**Results:** During the study period 148 of 174 women were hospitalized due to PID or TOA. The mean age was 35.7 ±9.3 years and mean duration of hospitalization was 5.9 ±3.7 days. Women with (n=21; group 1) and without (n=127; group 2) endometriosis were compared. Women in group 1 were significantly more likely to have undergone a fertility procedure prior to being admitted (9/27 (45%) vs. 22/121 (17%), p<0.001); particularly in vitro fertilization (IVF) (7/ 27 (33%) vs. 12/121 (9%), p<0.006); Women in group 1 more frequently experienced a severe and complicated course involving longer duration of hospitalization (8.8 ± 4.7 vs. 4.4 ± 2.3 days, p<0.0001), and antibiotic treatment failure (10/27 (48%) vs. 8/121 (6%), p<0.0001).

**Conclusion:** PID in women with endometriosis is more severe and refractory to antibiotic treatment, often requiring surgical intervention. It is likely that endometriosis is a risk factor for the development of severe PID, particularly after IVF treatment.

**Keywords:** Endometriosis, PID, TOA

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S9-6

**ENDOMETRIOTIC WOMEN PRESENT AN INCREASED PREVIOUS SPONTANEOUS ABORTIONS RATE**

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**Objectives:** To evaluate the first trimester pregnancies outcomes: previous spontaneous abortions (PSA), induced abortions and ectopic pregnancies in women with endometriosis as compared to unaffected women.

**Design:** We conducted a cross sectional study in a tertiary-care university hospital between January 2004 and March 2013. This study enrolled a cohort of 1851 patients: 870 with histologically proven endometriosis and 981 unaffected women. A thorough surgical examination of the abdominopelvic cavity was performed in all study participants.

**Materials and Methods:** Data were collected preoperatively using a structured questionnaire. Among women who conceived before the surgery, the type and number of the different previous first trimester pregnancies outcomes were studied. PSA rate was studied according to the existence of previous infertility history and the disease severity (rAFS and surgical classification).

**Results:** Endometriotic women were more likely to be nulligravida as compared to controls (585/870 (67.3%) vs 513/981 (52.4), respectively;  $p < 0.001$ ). Among women who conceived (284 endometriotic women and 466 controls) previous spontaneous abortion rate is significantly increased in women with endometriosis as compared to controls (139/478 (29%) vs 187/964 (19%), respectively;  $p < 0.001$ ). After subgroup analysis PSA rates of women with endometriosis and controls are respectively: 20% vs 12% ( $p = 0.003$ ) among women without previous history of infertility, 53% vs 30% ( $p < 0.001$ ) in case of previous history of infertility, and finally 58% vs 33% ( $p < 0.001$ ) among women with previous infertility and assisted reproductive treatment (ART). No effect of the disease severity (using rAFS stages or the surgical classification) was observed on spontaneous abortion rate.

**Conclusion:** Endometriotic women display significantly higher previous spontaneous abortion rate than disease free controls independently of the existence of previous history of infertility or disease severity.

**Keywords:** Pregnancy-outcome, endometriosis, spontaneous-abortion

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**S9-7**

**BENEFITS OF ORAL CONTRACEPTIVES IN DYSMENORRHEA AND DYSPAREUNIA: CASE-CONTROL STUDY IN MEDICAL STUDENTS OF COIMBRA UNIVERSITY, PORTUGAL**

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**Objectives:** Evaluation of the impact of oral contraceptives (OC) in young women clinically suspected of endometriosis.

**Design:** Data was gathered by the use of a questionnaire specially designed for the purpose of this study, comparing two groups: G1 (medical students – study group) and G2 (healthy women blood donors - control group). Intensive dysmenorrhea, dyspareunia and type of OC were evaluated.

**Materials and Methods:** This case-control study included 670 medical students in G1 and 700 blood donors in G2. Two subgroups were performed: (A) women with dysmenorrhea, (B) women with dyspareunia. Several parameters were analyzed in order to compare both groups. Statistical analysis was performed using SPSS version 17.0®.

**Results:** On what concerns epidemiologic data, groups were similar except for social, cultural stratification and stress level – significantly higher on what concerns medical students. Pain control was achieved in OC users, but a significant statistical difference was observed when comparing G1 [(A) 93.3%,  $p < 0.001$  and (B) 92%,  $p = 0.001$ ] and G2 [(A) 91.7%,  $p < 0.001$  and (B) 88.9%,  $p = n.s.$ ]. The results obtained were not related to different progestins or the dose of ethinyl estradiol ( $p = n.s.$ ) despite the majority of women in both groups referring pain relief used OC containing 19-nortestosterone derivatives and  $\leq 20\mu\text{g}$  of ethinyl estradiol. Dysmenorrhea, dyspareunia, or both were significantly reduced in medical students group in comparison to blood donors.

**Conclusion:** Oral contraceptives are an important choice for relief of endometriosis suggestive symptoms, being an useful method in order to improve life quality in these women. In our data this is true for superior socio-cultural women, under higher stress levels, suggesting a relation between life style and endometriosis prevalence.

**Keywords:** Endometriosis, dysmenorrhea, dyspareunia

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S10-1

**OVEREXPRESSION OF P27KIP1 IN CULTURED ENDOMETRIAL CELLS FROM PATIENTS WITH ENDOMETRIOSIS NORMALIZES ANGIOGENIC FACTORS EXPRESSION.**

Giovana Gonçalves<sup>1</sup>, [Adriana Invitti](#)<sup>1</sup>, Rafael Parreira<sup>1</sup>, Fernando Yasanuma<sup>1</sup>, Manoel Girão<sup>1</sup>, Eduardo Schor<sup>1</sup>

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**Objectives:** In this study we tested the hypothesis that overexpression of p27kip1 in cultured primary human endometrial cells from women with endometriosis normalizes inflammatory cytokines and VEGF expression.

**Design:** First generation bicistronic adenovirus: AdCMVhp27IRESEGFP (Adp27) and AdCMVNull (AdNull) were engineered in order to induce p27 expression in endometrial cells. The effect of Adp27 was assessed in primary cultures of endometrium of women with and without endometriosis during the period of 1 and 7 days after adenovirus transduction.

**Materials and Methods:** We examined the effect of p27kip1 overexpression in endometrial cells of women with and without endometriosis in inflammatory cytokines and VEGF expression using a flow cytometry technique.

**Results:** In the endometriosis group, significant inhibition of Il-8 and VEGF expression was observed 1 and 7 days after p27kip1 overexpression to levels strikingly similar to those observed in the endometrium cells from women without endometriosis ( $p < 0.001$  for both). These results suggest that the p27kip1 protein overexpression can bring Il-8 and VEGF to normal expression.

**Conclusion:** In addition, these finding, strongly suggest, that the eutopic endometrium of women with endometriosis already harbor a peculiar genetic background.

**Keywords:** p27, VEGF, Il-8

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S10-2

**EPIGENETIC AND GENOMIC ANALYSES OF HUMAN FETAL MEMBRANES FROM PREGNANT ENDOMETRIOSIS-AFFECTED WOMEN**

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**Objectives:** Because of original observations of endometriotic-like nodules within the choriodecidua of fetal membranes from pregnant women affected with severe endometriosis, we further study the transcriptome and the difference in methylation over the genome of choriodecidua in such conditions as compared to choriodecidua from unaffected women.

**Design:** A case-control laboratory study in a tertiary-care university hospital. Fetal membranes were collected after a planned C-section at term from pregnant women, affected with severe endometriosis, and from control subjects. Choriodecidua were characterized by immunohistochemistry. Microarray analyses of the transcriptome and the methylome of cases vs. controls were conducted.

**Materials and Methods:** Immunohistochemistry analyses were performed on 12 choriodecidua from endometriosis affected-women and controls. Gene expression and DNA methylation were assessed on 3 pools of 3 sets of samples using Nimblegen-Chip Microarray and Infinium HumanMethylation450-BeadChip Illumina, respectively. Analyses were conducted using R/Bioconductor and Genomatix softwares and compared to ectopic endometriosis expression profile.

**Results:** Histological examination of fetal membranes from pregnant women affected with severe endometriosis demonstrated disseminated glandular components in choriodecidua surrounded by enlarged decidualized cells along the entire fetal membrane surface. 2177 genes were significantly deregulated (variation of expression > 2, p.value < 0.05). Non-supervised hierarchical clustering of these genes confirmed a differential gene profile enriched for processes toward gland process, endocrine system, nervous system, and autoimmune disease. 611 genes were found common deregulated as compared to in ectopic endometriosis, coding for autoimmune disease of the nervous system and Endometriosis. CpG methylation analysis revealed 1177 differential methylated regions (DMR) with a p.value threshold <0.001, mainly in the chromosome 6 (13%) which contains the HLA locus.

**Conclusion:** The hormonal ovarian blockade occurring during pregnancy appears to be not sufficient to prevent development of endometriotic tissue into the choriodecidua layer of fetal membranes. This suggests endometriotic lesions preserve their invasive capacities during pregnancy, in a very specific immunological environment inherent of the pregnant uterus.

**Keywords:** Choriodecidua, transcriptome, methylome

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S10-3

**GENOME-WIDE ANALYSIS OF METHYLOME REVEALS LARGE EPIGENETIC ALTERATIONS IN ENDOMETRIOSIS**

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**Objectives:** The establishment of endometriotic lesions appears to be driven by epigenetic alterations. Some data have been accumulated on key genes showing differential methylation status of their promoter in the lesion as compared to the eutopic endometrium. However the extent of the epigenetic alterations at the genome level is largely unknown.

**Design:** We proposed to compare the methylome of the endometriotic lesion and the matched eutopic endometrium.

**Materials and Methods:** We screened three endometriomas and matched endometrium using 450K Illumina Infinium array. We analyzed windows of 10 consecutive CpG on a chromosome-wide basis with p-values considered significant following a Monte-Carlo simulation. We validated ten genes harboring differential methylation profile by enzymatic digestion and qPCR in 8 independent samples.

**Results:** A total of 277 regions significantly hypomethylated or hypermethylated were identified near or inside 312 genes. There was an excellent correlation between the differences of the methylation levels in the microarray and the qPCR validation (R=0.875). We could report three major results: (i) Differential methylation concentrated near chromosome ends; (ii) Differential methylation in endometrioma was often associated with gene expression deregulation, but did not foretell the sense of the deregulation; (iii) Differential methylation in endometriomas affects a very high proportion of transcription factors with a significant clustering of genes involved uterine neoplasms and centered on Estrogen Receptor 1 (ESR1).

**Conclusion:** This study demonstrates the existence of wide epigenetic alterations in endometriosis and unveils new genes potentially implicated in endometriosis pathogenesis.

**Keywords:** methylome, ESR1, endometrioma

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S10-4

**ABERRANT DNA METHYLATION PROFILES AND PATTERNS OF HUMAN EUTOPIC ENDOMETRIUM IN ENDOMETRIOSIS AND ITS ASSOCIATION WITH OTHER REGULATORY ELEMENTS**

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**Objectives:** We previously found the DNA methylome of human eutopic endometrium changes across the cycle with abnormalities in endometriosis. Preliminary comparison with gene expression changes also showed pathway differences. Herein, we investigated genomic characterization of abnormally methylated loci in each phase to elucidate mechanisms of epigenetic (de)regulation of transcription in endometriosis.

**Design:** Eutopic endometrial tissue from proliferative (PE), early secretory (ESE), and mid-secretory (MSE) phases from women with and without endometriosis (severe) were globally arrayed for DNA methylation and gene expression. Comprehensive genomic characterization and gene expression association were investigated for differentially methylated loci for each phase in disease vs. no disease.

**Materials and Methods:** Samples were obtained from the UCSF NIH Human Endometrial Tissue/DNA bank. Illumina Infinium 27K and Affymetrix HU133 were used for profiling. R programming, DAVID, ENCODE and UCSC databases, IPA, JASPAR, MAPPER and other programs were used for statistical analysis, loci characterization, and association with transcription factors and histone modifications.

**Results:** Greatest DNA methylation differences in disease vs. no disease occurred in secretory endometrium and less extensively in PE. Association of DNA methylation and transcription changes were assessed further based on CpG sites' genomic location, CpG islands (CGIs), splicing/promoter variants, transcription factor binding sites (TFBS) and histone modifications. In ESE and MSE, most aberrant methylation occurred at CGIs with either positive or negative association with transcription, different from PE with mostly negative association and involving both CGIs and non-CGIs. In all phases, most changes at non-CGIs when located at promoters were negatively associated with transcription. For CGIs, positive or negative association with transcription was mostly dependent on CpG site genomic location. For several loci, we found potential TFBSs and histone modifications associated with the observed abnormalities.

**Conclusion:** Extensive DNA methylation abnormalities in secretory endometrium may reflect the progesterone-resistance phenotype in endometriosis. The nature of DNA methylation abnormalities with respect to genomic location, potential involvement of transcription factors and histone modifications suggests a complex interplay of these regulatory elements in aberrant transcriptional regulation observed in endometriosis.

**Keywords:** Epigenetics, Endometrium, Endometriosis

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S10-5

**VARIABILITY OF GENOME-WIDE GENE EXPRESSION AND DNA METHYLATION VALUES ACROSS TISSUE SAMPLES FROM WOMEN WITH AND WITHOUT ENDOMETRIOSIS.**

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**Objectives:** Large-scale expression and DNA methylation analyses in tissues relevant to endometriosis are required for de-novo investigations of pathogenesis, and follow-up of implicated genomic regions. To inform future study design, we investigated intra- and inter-tissue variability of genome-wide expression and methylation between three tissues, and the influence of tissue collection/processing parameters.

**Design:** Twenty-four individuals enrolled in ENDOX (8 endometrioma cases; 8 with peritoneal endometriosis; 8 controls) provided 48 tissue samples collected during laparoscopy using standardized protocols (16 eutopic, 16 ectopic endometrium; 16 subcutaneous adipose tissue). Subjects were not using hormones and had regular cycles; controls were frequency-matched to cases on menstrual phase.

**Materials and Methods:** Tissues were split for DNA vs. RNA extraction. In each extraction arm, the 32 eutopic and ectopic endometrium and 8/16 adipose tissue samples were split prior to extraction; 10% of samples were analysed in duplicate. DNA and RNA samples (n=96 each) were analysed using Illumina 450Kmethylation and H12 expression arrays.

**Results:** Sample weights varied from 140 to 776 mg for endometriomas, 32 to 233 for peritoneal endometriosis, 43 to 572 mg for eutopic endometrium, and 30 to 665 mg for adipose tissue. DNA and RNA yield and concentrations were predominantly determined by tissue type ( $P < 0.001$ ), with adipose tissue providing the lowest yields (DNA mean 533ng (SD: 344); RNA mean 452 ng (SD: 301)) and eutopic endometrium the highest (DNA mean 4245 ng (SD: 1942); RNA mean 4516 ng (SD: 3100)). After adjusting for tissue type, tissue weights did not significantly correlate with DNA or RNA yields or concentrations. Analyses of genome-wide expression and methylation profiles and their variability within tissues and according to protocol-related and QC parameters are currently underway and will be presented.

**Conclusion:** Our results will enable appropriate study design of future large-scale collaborative studies of genome-wide and targeted expression and methylation, and will inform the standardized tissue collection and processing protocols generated and continuously updated by the WERF Endometriosis Phenome and biobanking Harmonisation Project (EPHect).

**Keywords:** Epigenetics, Methylation, Expression

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S10-6

**AN ITALIAN ASSOCIATION STUDY CONFIRMS PREVIOUS GWAS DATA SUPPORTING VEZT AS SUSCEPTIBILITY LOCUS FOR ENDOMETRIOSIS**

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**Objectives:** This study was aimed to confirm whether SNP rs10859871 near VEZT, SNP rs13394619 in GREB1, SNP rs4141819 at 2p14 and SNP rs61764370 in let-7 microRNA binding site in KRAS were associated with endometriosis. Three of these SNPs derive from the meta-analysis of two GWA studies in Japanese and Anglo-Australian populations.

**Design:** We conducted a replication Italian case-control association study involving an independent set of 274 patients with laparoscopically proven endometriosis and 273 controls in whom endometriosis was laparoscopically ruled out. The four SNPs - rs10859871, rs13394619, rs4141819 and rs61764370 - were selected and genotyped for this association study.

**Materials and Methods:** SNPs rs10859871, rs13394619 and rs4141819 were genotyped using Taq-Man pre-designed SNP genotyping assay from Applied Biosystem Inc. SNP rs61764370 was sequenced using a standard method due to the difficulties in probe design.

**Results:** We found a strong genetic association between VEZT rs1085987 and endometriosis (OR 1.58; 95% CI 1.24-2.02,  $p=2.0 \times 10^{-4}$ ) in the Italian population. Conversely, no association was found for GREB1 rs13394619 and rs4141819 in 2p14. Moreover we confirm previous findings indicating absence of association for rs61764370 in let-7 binding site.

**Conclusion:** We have confirmed VEZT as a susceptibility locus for endometriosis. VEZT gene is a plasma membrane component of adherens junctions. The intracellular domain of VEZT binds to myosin VIIA. VEZT functions as an adherens junction transmembrane protein, but the exact role of VEZT gene is currently unknown.

**Keywords:** Let7, VEZT, association

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S10-7

**VALIDATION OF HISTONE 3 AND HISTONE 4 LYSINE TRI-METHYLATION STATUS OF ENDOMETRIOSIS LESIONS**

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**Objectives:** We have previously shown that endometriotic lesions have a distinct profile of histone trimethylation profile using commercial immunoassays. The aim of this study was to validate our previous data using Western Blot (WB)

**Design:** Design: Case-Control study. The histone modification profiles of an independent set of tissues from patients and controls were determined by WB and correlated with immunoassay results.

**Materials and Methods:** Fresh tissues (9 lesions, 9 endometrium from patients, 9 controls) collected at surgery were pathologically evaluated and mechanically dispersed. Protein level results were correlated with previously obtained data using immune-based assay (Epigentek).

**Results:** WB analysis performed in eutopic and ectopic endometrium showed different patterns of histone marks (H3K4me3, H3K9me3, H3K27me3, H3K36me3, H3K79me3, H4K20me3). WB analysis confirmed our previous observation of lower levels of the H3K4me3 mark in endometriotic tissues vs. controls. The H3K4me3 histone modification is a well-known active histone mark, i.e., it induces transcription of target genes. We have also conducted bioinformatic analyses to identify areas of enrichment for H3K4me in promoter regions of candidate genes for endometriosis, including ESR1, CDH1, p21, HOXA10, and SF1. Except for SF1, these genes are under expressed in endometriosis lesions, therefore we speculate that they are subject to transcriptional regulation by H3K4me3. Ongoing studies include chromatin immunoprecipitation (ChIP)-PCR studies to identify promoter regions of candidate genes for endometriosis.

**Conclusion:** Our results provide further evidence to document the lower levels of H3K4me3 in endometriotic lesions as compared to eutopic endometrium from patients and controls. H3K4me3 is associated with active chromatin and transcription of target genes. Our data can help better understand the role of epigenetics in the pathophysiology of endometriosis

**Keywords:** Endometriosis, Histone, Epigenetics

Saturday 3 May 2014

Video Session #2

V2-1

**A NEW EXCISION PROCEDURE FOR LOW AND MID RECTAL ENDOMETRIOSIS NODULES USING COMBINED TRANSANAL AND LAPAROSCOPIC APPROACH**

Horace Roman<sup>1</sup>, Jean-Jacques Tuech<sup>1</sup>

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**Objectives:** To report preliminary results of a new technique for transanal full thickness disc excision of rectal endometriosis nodules.

**Design:** Prospective series of patients undergoing a new surgical procedure.

**Materials and Methods:** Patients benefited from the combined laparoscopic and transanal excision of rectal nodules using the Contour Transtar stapler (Ethicon Endosurgery Inc). First, the rectal area infiltrated by the nodule was shaved, then the general surgeon seized the shaved area into the transanal stapler jaws and performed a large disc excision.

**Results:** The procedure was successfully performed in 12 women with symptomatic deep endometriosis infiltrating the low- and mid-rectum. They represented 7.5% of 162 women managed during this same period by various procedures for rectal nodules. The height of the nodules ranged from 40 to 100 mm above the anus (median 60 mm). The postoperative follow up ranged from 6 to 43 months (median 26 months). The largest diameter of specimens varied from 40 to 80 mm (55±11 mm). The postoperative follow up ranged from 6 to 43 months (median 26 months). One rectovaginal fistula was recorded in a patient undergoing large vaginal resection. Median postoperative value for the Gastrointestinal Quality of Life Index and the Knowles-Eccersley-Scott-Symptom Questionnaire was 114±15 (range 90-137) and 8±7 (range 1-20) respectively.

**Conclusion:** Our data suggest that this new technique of transanal rectal disc excision using the contour stapler may be applied in patients with infiltrating endometrial nodules of the rectum up to 10 cm from the anal margin and up to 5 cm in diameter, thus it specifically avoids low colorectal resections.

**Keywords:** Rectal endometriosis; excision

Saturday 3 May 2014

Video Session #2

V2-2

**CASE REPORT OF ABDOMINAL WALL ENDOMETRIOSIS MANAGED LAPAROSCOPICALLY**

Joao Alves<sup>1</sup>, Rodrigo Fernandes<sup>2</sup>, Maria Arque<sup>3</sup>, Aline Host<sup>4</sup>, Marco Puga<sup>5</sup>, Arnaud Wattiez<sup>2</sup>

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**Objectives:** To describe in a surgical video the management of abdominal wall endometriosis

**Design:** Case report of a 35 years old woman with abdominal wall endometriosis

**Materials and Methods:** We recorded the video in live surgery in Strasbourg and edited to present the key points of laparoscopic treatment of abdominal wall endometriosis

**Results:** We present a clinical case of a 35 years-old woman with cyclic upper right quadrant abdominal pain (coinciding with menses) 6 months after stopping her birth control pills. We found 6X1,5X3 cm mass close to liver's VI segment in the right transverse muscle. Surgery was feasible by laparoscopy with complete resection of the mass. a Histological analysis was consistent with abdominal wall endometrioma. Patient is without symptoms 4 months after the surgery.

**Conclusion:** Surgical treatment is the treatment of choice for these patients and in our patient laparoscopy was feasible.

**Keywords:** Abdominal wall endometrioma

Saturday 3 May 2014

Video Session #2

V2-3

**SURGICAL TREATMENT OF BLADDER ENDOMETRIOSIS ASSOCIATED WITH EXTERNAL ADENOMYOSIS**

Luciano Gibran<sup>1</sup>, Patrick Bellelis<sup>1</sup>, Marco Antonio Bassi<sup>1</sup>, Luiz Flavio Cordeiro Fernandes<sup>1</sup>, Sergio Podgaec<sup>1</sup>, Mauricio Simoes Abrao<sup>1</sup>

<sup>1</sup> University of Sao Paulo, Sao Paulo, Brazil

**Objectives:** To describe the approach of vesical endometriosis associated with external adenomyosis.

**Design:** a case report in a 33 - year old patient with cyclic urinary symptoms such as dysuria and hematuria, and chronic pelvic pain and recurrent urinary infections. The transvaginal/transabdominal ultrasound with prior bowel preparation identified the presence a nodule with 3,5cm infiltrating all the vesical wall.

**Materials and Methods:** it was performed a videolaparoscopy with adhesiolysis in order to distinguish the lesion from other bladder structures. After this, we promoted the resection of endometriotic nodule starting from the healthy tissue around it and than the suture in two layers. At the end, metilene blue was instilled to identify leakage.

**Results:** The surgery proceeded without any complications and with minimal blood loss. The duration of the procedure was 55 minutes. On day one after surgery received discharge without pain. We have maintained the patient with an open Foley catheter No. 14 for 10 days postoperatively. In the late postoperative period, the patient showed improvement in the pelvic pain and no loss on urinary function.

**Conclusion:** Lesions of the urinary tract are not associated. Endometriosis of the ureter is extrinsic and is related to bowel disease meanwhile vesical endometriosis is an intrinsic disease. Adenomyosis external, whose involvement occurs from the uterine serosa, is usually related with deep endometriosis lesions in adjacent organs.

**Keywords:** Endometriosis, bladder, treatment

Saturday 3 May 2014

Video Session #2

V2-4

**ROBOTIC APPROACH FOR THE TREATMENT OF THE OVARIAN ENDOMETRIOMA - THE TECHNIQUE**

Duarte Ribeiro<sup>1</sup>, Paulo Serafini<sup>2</sup>, Gladis Ribeiro<sup>1</sup>, Thiago Pareja<sup>1</sup>, Luciana Chamié<sup>3</sup>, Rogério Leão<sup>1</sup>

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**Objectives:** The purpose of this video is to present a technique of a robotic cystectomy in order to increase the preservation of the ovarian function as much as possible and decreasing the recurrence rate.

**Design:** Serial cases results.

**Materials and Methods:** 75 ovaries were submitted a robotic cystectomy, using the same technique, performed by the same surgeon. The technique applied follows the principles disseminated by Professor Canis, but adapted to the robotic system. The surgeries were performed in two hospitals, of high complexity, in Sao Paulo, Brazil, since 2010.

**Results:** From the 75 ovaries operated with resection of the fourth zone, there was not any injuries in the ureter or in the ovarian vessels, nor any other complications, obtaining positive results for anatomic pathological endometriosis in the fourth zone in 92% of cases under analysis. However, until now, the study is inconclusive regarding the improve of the function of preserving ovarial funcion, due to the period of follow-up short and low number of cases.

**Conclusion:** The technique is safe, easily reproducible and has low morbidity, allowing surgeons to apply what is already known: the best treatment is the complete removal of all visible disease. Despite the short time and cases under analysis, the study holds promise to its initial claim.

**Keywords:** Endometrioma; Robotic; Cystectomy;

Saturday 3 May 2014

Video Session #2

V2-5

**STANDARDIZATION OF VIDEOLAPAROSCOPIC SURGERY FOR DEEP ENDOMETRIOSIS BY  
COLORECTAL SURGEON**

Univaldo Sagae<sup>1</sup>, Doryane Lima<sup>2</sup>, Gustavo Kurachi<sup>3</sup>, Namir Cavalli<sup>3</sup>, Danilo Galetto<sup>4</sup>, Milton Tanaka<sup>5</sup>

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**Objectives:** To provide guidelines for colorectal surgeons using videolaparoscopy (VL) in the treatment of patients with DE involving the rectosigmoid colon.

**Design:** Patients with DE referred by the outpatient gynecology service to the Department of Colorectal Surgery due to gastrointestinal complaints were submitted to thorough physical evaluation (rectal and vaginal digital examination) and 3D anorectal ultrasonography (3D US). Patients with intestinal involvement on 3D US were treated with multidisciplinary VL surgery.

**Materials and Methods:** Following adaptation and standardization of videolaparoscopic surgery for pelvic DE over the last 3 years, complete resection rates were found to have improved (confirmed by anatomopathological examination), resulting in reduced rates of surgical, urological and gastrointestinal complications

**Results:** Careful manipulation of gynecological organs, with the presence of a gynecologist throughout the surgery was important step. The surgeon preserved upper rectal artery and NOTES was used as an option (possibility of vaginal access for perioperative digitation, manipulation, opening and excision of surgical specimens). Adequate handling of stapler for resection of different types of rectosigmoid colon infiltration. Following adaptation and standardization of videolaparoscopic surgery for pelvic DE over the last 3 years, complete resection rates were found to have improved (confirmed by anatomopathological examination), resulting in reduced rates of surgical, urological and gastrointestinal complications.

**Conclusion:** The use of the above guidelines makes it possible to standardize VL surgery for DE with reproducibility among colorectal surgeons and thereby reduce the duration of surgery and the rate of complications and recurrence.

**Keywords:** Videolaparoscopy; rectosigmoid colon

Saturday 3 May 2014

Video Session #2

V2-6

**STAGE IV ENDOMETRIOSIS AND LEFT UTEROLYSIS**

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<sup>1</sup>Centre for Advanced Reproductive Surgery (C.A.R.E), Sydney, Australia, <sup>2</sup>Centre for Advanced Reproductive Endosurgery, Sydney, Australia

**Objectives:** Left ureterolysis Right pararectal space dissection Excision of endometriosis form L USL/Pararectal space to RVS to R USL/Pararectal space

**Design:** severe posterior vaginal and RVS fibrotic disease close to anal sphincter

**Materials and Methods:** Cystoscopy,insertion of left ureteric stent

**Results:** laparoscopic excision of stage IV endometriosis adenomyosis of the posterior Cervix, Left uterine artery secured at its origin left uterolysis cystoscopy,insertion of left ureteric stent ( double-j stent passed into left hydroureter resulted in immediate decompression,stent left in situ Repair of inadvertent cystotomy in the dome of bladder ,closed using 2-0- vicryl laparoscopic-assisted ultra low anterior resection of rectum rectum mobilised,IMA spared tension-free colo-anal anastomosis and the use of Echelon flex 45Gx3 to rectum,double stapled sigmoidoscopy and air insufflation test performed to confirm integrity of anastomosis

**Conclusion:** laparoscopic excision of stage IV

**Keywords:** excision of endometriosis

**Saturday 3 May 2014**  
**Video Session #2**

**V2-7**

**UPDATE ON ROBOTICS AND ENDOMETRIOSIS – WHAT IS THE CURRENT STATE?**

Charles Miller<sup>1</sup>

<sup>1</sup> United States

**Objectives:** Robotic surgery has proven to be a viable alternative for the treatment of many gynecologic disorders. Excellent patient outcomes have been noted both in the management of gynecologic malignancies as well as benign pathologic conditions.

**Design:** This is a review of our current understanding of robotic assisted surgery for endometriosis as well as a literature review on this emerging surgical alternative for the treatment of both superficial and deep infiltrative endometriosis.

**Materials and Methods:** Robotic surgery has proven to be a viable alternative for the treatment of many gynecologic disorders. Excellent patient outcomes have been noted both in the management of gynecologic malignancies as well as benign pathologic conditions.

**Results:** Robotic surgery has proven to be a viable alternative for the treatment of many gynecologic disorders. Excellent patient outcomes have been noted both in the management of gynecologic malignancies as well as benign pathologic conditions. This includes both oncologic as well as benign hysterectomy, lymph node dissection, myomectomy, sacrocolpopexy, and tubal anastomosis. The last frontier would appear to be the treatment of endometriosis. This is a review of our current understanding of robotic assisted surgery for endometriosis as well as a literature review on this emerging surgical alternative for the treatment of both superficial and deep infiltrative endometriosis.

**Conclusion:** Robotic surgery has proven to be a viable alternative for the treatment of many gynecologic disorders.

**Keywords:** Robotics

## Poster - Adenomyosis

P-01

### CAN MINIMALLY INVASIVE SURGICAL TREATMENT OF ADENOMYOSIS BE AN ALTERNATIVE TO HYSTERECTOMY OR HORMONAL TREATMENT?

Dmitriy Bryunin<sup>1</sup>, Alla Bakhvalova<sup>1</sup>, Yuliya Romadanova<sup>1</sup>, Anatoliy Ischenko<sup>1</sup>

<sup>1</sup> First Moscow State Medical University named after I.M.Sechenov, Moscow, Russia

**Objectives:** Estimation of the effectivency of organ-saving surgical methods of treatment of adenomyosis.

**Design:** This investigation was realised prospectively.

**Materials and Methods:** 89 women with adenomyosis aged 33-51 were examined and underwent organ-saving operations. 7 patients underwent endometrial ablation, 58 patients - endoscopic laser-induced interstitial thermotherapy with laparoscopic clipping of internal iliac arteries and 24 - resection of adenomyotic nodules. The follow-up period was 1-7 years.

**Results:** The only patients who were absolutely content with the results of treatment were the patiens who underwent the resection of singular adenomyotic nodule. They noted the total relief of pain syndrome. Other patients who underwent endometrial ablation or endoscopic laser-induced interstitial thermotherapy with laparoscopic clipping of internal iliac arteries noted the reduction of menstrual bleeding and pain for some time, but then the symptoms come back that demand some kind of hormonal treatment. Nearly one third of the patients needed subsequent radical surgical treatment during the follow-up period.

**Conclusion:** The effectiveness of organ-saving surgical methods of treatment of adenomyosis such as endometrial ablation and endoscopic laser-drilling with laparoscopic clipping of internal iliac arteries is controversial. The hormonal therapy can be a method of choice especially for young women, hysterectomy is a method of choice for premenopausal patients.

**Keywords:** Adenomyosis, treatment.

## Poster - Adenomyosis

P-02

### ACTIVINS AND ADENOMYOSIS

Patrizia Carrarelli<sup>1</sup>, Pasquapina Ciarmela<sup>2</sup>, Lucia Funghi<sup>1</sup>, Felice Arcuri<sup>1</sup>, Claudia Tosti<sup>1</sup>, Felice Petraglia<sup>1</sup>

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**Objectives:** Adenomyosis is characterized by presence of ectopic endometrial glands and stroma in the myometrium. We evaluate activin-betaA and -betaB subunits mRNA expression in matched endometrium, myometrium and adenomyosis collected from women with adenomyosis, to investigate activins involvement in myometrial pathophysiology and their possible relationship with adenomyosis.

**Design:** Patients with adenomyosis afferent to the Department of Obstetrics and Gynecology of University hospitals in Siena (Italy).

**Materials and Methods:** Tissues of matched myometrium, endometrium and adenomyosis (ectopic endometrium) were obtained from patients with adenomyosis (n=6) who underwent hysterectomy. Total RNA was extracted from tissue homogenates and gene expression analyzed by quantitative Real Time-PCR.

**Results:** Activin-betaA subunit mRNA expression in ectopic endometrium of patients with adenomyosis was two-fold higher than in matched eutopic endometrium, while its expression was similar to matched normal myometrium. Activin-betaB subunit mRNA expression was substantially increased (three-fold) in ectopic endometrium of patients with adenomyosis compared to both matched endometrium and myometrium.

**Conclusion:** Our data showed an up-regulation of both activin-betaA and -betaB subunits mRNA expression in adenomyosis. The altered mRNA expression of both activins subunits in ectopic tissues observed in our patients supports the involvement of the TGF-beta family members, in particular activins, in the pathogenesis of adenomyosis.

**Keywords:** Adenomyosis, activin

## Poster - Adenomyosis

P-03

### PRE AND POST-OPERATIVE CLINICAL AND TRANSVAGINAL ULTRASOUND FINDINGS OF ADENOMYOSIS IN PATIENTS WITH DEEP INFILTRATING ENDOMETRIOSIS

Lucia Lazzeri<sup>1</sup>, Alessandra Di Giovanni<sup>2</sup>, Caterina Exacoustos<sup>3</sup>, Mario Malzoni<sup>2</sup>, Felice Petraglia<sup>1</sup>, Errico Zupi<sup>1</sup>

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**Objectives:** The present study investigated the possible presence of adenomyosis in a group of women with DIE and its impact on pre and postoperative symptoms.

**Design:** Prospective multicenter study developed in three Endometriosis centers in Italy

**Materials and Methods:** Women laparoscopically positive for DIE (n=121) were enrolled and clinical and ultrasound evaluations were performed for the preoperative assessment. Dysmenorrhea, dyspareunia, abnormal uterine bleeding, bowel and urinary symptoms were considered. In a subgroup (n=55) a follow-up evaluation was done within 3/6 months after surgery.

**Results:** A relevant number of patients with DIE showed adenomyosis (n=59; 48.7%); in this group dysmenorrhea ( $p=0.0019$ ), dyspareunia ( $p=0.0004$ ), and abnormal uterine bleeding ( $p<0.001$ ) were statistically higher in than the DIE group. After surgery painful symptoms improved in the whole group, but remained significantly higher ( $p<0.001$ ) in the group with adenomyosis.

**Conclusion:** Adenomyosis is frequently associated with DIE and significantly affects pre and post-operative symptoms, thus influencing the follow up management.

**Keywords:** adenomyosis, DIE, TVS

## Poster - Adenomyosis

P-04

### DISTRIBUTION OF NERVE FIBERS IN ADENOMYOSIS AND ITS CLINICAL SIGNIFICANCE

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**Objectives:** To investigate nerve fibers' distribution in adenomyosis and their relationship with dysmenorrhea.

**Design:** A case control study collecting tissue of 64 patients from August 2009 to August 2010.

**Materials and Methods:** Myometrium was sampled from 64 hysterectomy specimens. including 40 cases with adenomyosis and 24 cases with cervical intraepithelial neoplasia as control. They were stained immunohistochemically for PGP9.5, S-100, NF, NSE, SP-immunoreactive nerve fibers respectively.

**Results:** The positive rate of SP immunoreactive nerve fibers in the myometrium were 70% (28/40) in adenomyosis and 29.12%(7/24) in the control group. And their density were (0.70 0.32 )/mm<sup>2</sup> and (0.24 0.21)/mm<sup>2</sup> with statistical differences (P<0.05). NF immunoreactive nerve fibers and the nerve density in the myometrium were 92.5%(37/40) and (1.44 0.98)/mm<sup>2</sup> in adenomyosis, which was significantly higher than 20.8%(5/24) and (0.31 0.29)/mm<sup>2</sup> in the control group (P<0.05). Moreover, the density of NF immunoreactive nerve fibers in adenomyosis was positively correlated with the severity of pain (r=0.703, P<0.05). However, there were no statistical different S-100, NSE and PGP9.5 immunoreactive nerve fibers distribution between the two groups (P>0.05).

**Conclusion:** NF and SP immunoreactive nerve fibers might confer the mechanism of pelvic pain with adenomyosis.

**Keywords:** Adenomyosis; Nerve fibres; Immunohistochemistry; Dysmenorrhea

## Poster - Adenomyosis

P-05

### THE PREVALENCE OF SONOGRAPHIC SIGNS OF ADENOMYOSIS IN WOMEN UNDERGOING SURGERY FOR ENDOMETRIOSIS

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**Objectives:** To determine the prevalence of adenomyosis in women undergoing surgery for endometriosis at a large tertiary referral center, using transvaginal ultrasound.

**Design:** Retrospective analysis of stored ultrasound examinations of women assessed prospectively at a tertiary referral endometriosis center. A diagnosis of endometriosis which required surgery was made based on clinical criteria and findings at the time of the ultrasound scan.

**Materials and Methods:** All women underwent a transvaginal ultrasound scan with three dimensional capabilities by a single operator. Diagnosis of adenomyosis was made when any one of the following criteria was present: asymmetrical myometrial thickening, linear striations, myometrial cysts, hyperechoic islands, irregular endometrial-myometrial junction, parallel shadowing, and localized adenomyomas.

**Results:** 103 women underwent surgery, with mean age 34±6.1 years (20-47), median parity 1±1 (0-6), mean BMI 23.1±4 (16.9-35.5), 57 (55.5%) were nulliparous, 9 (8.7%) after cesarean sections. Symptoms included dysmenorrhea (91.5%), dyspareunia (59.6%), urinary complaints (25.3%), gastrointestinal complaints (50.5%) and infertility (31%). 24 (23.3%) underwent IVF treatments with 15 undergoing 3 cycles or more (1-16). At least one sonographic sign indicative of adenomyosis was observed in 88.4%: asymmetrical myometrial thickening (75.6%), linear striations (26.3%), myometrial cysts (85.3%), hyperechoic islands (80%), irregular endometrial-myometrial junction (86.3), parallel shadowing (57.9%), and localized adenomyomas (39%). The presence of sonographic findings was associated with age, dysmenorrhea, dyspareunia, and infertility. Histological confirmation of adenomyosis was unavailable as none of the women underwent a hysterectomy but endometriosis was confirmed in all.

**Conclusion:** Sonographic signs of adenomyosis are highly prevalent in women undergoing surgery for endometriosis. This bears direct implications on tailoring patient specific treatment both before and after the operation, such as secondary prevention or timing of fertility treatments.

**Keywords:** Adenomyosis, transvaginal ultrasound

## Poster - Adenomyosis

P-06

### PREOPERATIVE DIAGNOSTICS OF ADENOMYOSIS WITH PROTEOMIC SCREENING AND DETECTION THE INNATE IMMUNITY SYSTEM

Anna Sorokina<sup>1</sup>, Victor Radzinsky<sup>2</sup>, Marina Khamoshina<sup>2</sup>, Rustam Ziganshin<sup>3</sup>, George Arapidi<sup>3</sup>, George Totchiev<sup>4</sup>

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**Objectives:** The diagnosis of adenomyosis is complicated by the low specificity of its symptoms. The preoperative diagnosis of adenomyosis is only suggestive at best and most often is either not made or overdiagnosed. Exact diagnosis of adenomyosis only possible in posthysterectomy specimen.

**Design:** Peptidomic studies, i. e. total screening of biological samples for peptides is a rapidly growing field of biomolecular research. Many investigators have suggested that there is an association between the presence of adenomyosis and an altered innate immune system.

**Materials and Methods:** Comparative MALDI-TOF Mass Spectrometry profiling and spectrophotometry immunoassay (LE and alpha1-PI) of blood serum samples from patients with verified adenomyosis as well as from a control group of healthy women has been carried out.

**Results:** Classification models generated on the basis of respective MALDI-TOF Mass Spectrometry profiles demonstrated sensitivity and specificity close to 100% for the detection of adenomyosis. A number of peptide markers specific for adenomyosis have been revealed. The degree of LE activity is a prevalence rate of adenomyosis. The degree of alpha1-PI activity is correlated with antiproteolytic potential that blocks the effects shown by LE. It can lead the prognose of disease and timely treatment.

**Conclusion:** This study provides a potential diagnostic markers of adenomyosis, that can help make a prognosis and to lead adequate and timely treatment.

**Keywords:** Adenomyosis, proteomics, immunity

## Poster - Adenomyosis

P-07

### ASSOCIATION BETWEEN ENDOMETRIOSIS AND ADENOMYOSIS IN PATIENTS SUBMITTED TO HYSTERECTOMY

Carlos Souza<sup>1</sup>, Vanessa Genro<sup>1</sup>, Maria Lucia Oppermann<sup>2</sup>, Joelmir Chiesa<sup>1</sup>, Rita Chapon<sup>1</sup>, Joao Sabino Cunha Filho<sup>2</sup>

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**Objectives:** To evaluate the prevalence of endometriosis and epidemiological characteristics in a sample of patients submitted to hysterectomy with adenomyosis.

**Design:** Retrospective cross sectional study at an university hospital.

**Materials and Methods:** We performed a retrospective study of 58 patients submitted to abdominal or laparoscopic total hysterectomy with adenomyosis confirmed by anatomopatological evaluation between 2008 and 2012. We collected data about endometriosis diagnosis, epidemiological data and pain characteristics (analogovisual score).

**Results:** Forty patients were submitted to laparoscopic total hysterectomy and 18 patients submitted to abdominal hysterectomy, and 33(58.5) patients presented endometriosis diagnosis in our samples. Pain scores on group of endometriosis plus adenomyosis were higher than patients with adenomyosis only (dysmenorrhea  $6.3 \pm 2.5$  and  $2.7 \pm 2.9$   $p=0.001$ , dyspareunia  $5.27 \pm 3.43$  and  $2.3 \pm 2.7$ ,  $p=0.001$ ; pelvic chronic pain  $4.8 \pm 3.4$  and  $3.0 \pm 3.0$   $p=0.05$  t Test, respectively). In relation to age, height, weight and body mass index groups were not different. Patients with only adenomyosis were more parous than patients that presented endometriosis associated (gravity  $2.4 \pm 0.4$  and  $0.9 \pm 0.1$ , parity  $2.1 \pm 0.4$  and  $0.7 \pm 0.1$  - t Test, respectively).

**Conclusion:** Endometriosis is a frequent finding in patients with adenomyosis. Pain of patients with endometriosis associated to adenomyosis is more intense than in patients with adenomyosis only.

**Keywords:** Adenomyosis, endometriosis, hysterectomy

## Poster - Adenomyosis

P-08

### ADENOMYOSIS AND ADENOMATOID TUMOURS

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**Objectives:** To present laparoscopic excision of adenomyosis and two cases of adenomatoid tumors.

**Design:** At a University central hospital in Germany adenomyosis and adenomyotic tumour occur besides endometriosis excisions.

**Materials and Methods:** 1) Endometriotic lesions were biopsied and the pathohistological outcome was compared to the suspected diagnosis in 216 patients. 2) We performed histological diagnosis either by ultrasound guided needle biopsy or by endometrial resection or by needle biopsy during laparoscopy (n = 15). 3) Two women with uterine adenomatoid tumors.

**Results:** 1) In black and red lesions, including endometriomas, the suspected diagnosis was confirmed in >90% of cases and in white lesions in 53 %.2) In all patients we performed a laparoscopic resection. 3) Tumor excision is difficult because of the missing capsule. There is no clear plane of cleavage

**Conclusion:** : 1) Purely morphological criteria are not sufficient but these laparoscopic findings are still our most reliable points of reference. 2) Vaginal ultrasound combined with transabdominal or transvaginal myometrial biopsy established the diagnosis of adenomyosis in 15 infertility patients. 3) The proper laparoscopic handling of these tumors is crucial.

**Keywords:** Adenomatoid tumors, Adenomyosis

## Poster - Complementary therapies

P-09

### IN VITRO AND IN VIVO ENDOMETRIAL GROWTH INHIBITION BY NATURAL COMPOUNDS EVALUATED AS NEW THERAPEUTIC AGENTS FOR ENDOMETRIOSIS.

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**Objectives:** To evaluate the effect of Wogonin, an active constituent of Chinese Herbal Medicine; two of the main antioxidant compounds found in rosemary extract: Carnosic Acid (CA) and Rosmarinic Acid (RA); and 1 $\alpha$ ,25-dihydroxvitaminD3 (VD3) in vitro and in vivo, in experimental endometriosis. These compounds demonstrated antiproliferative properties in several cancer models.

**Design:** Stromal endometrial cells derived from endometriosis patients and the T-HESC cell line were cultured with Wogonin, CA or RA for 24-h, or VD3 for 48-h. Endometriosis was surgically induced in BALB/c mice. Animals were assigned randomly to different groups: RA-1mg/kg; RA-3mg/kg; CA-2mg/kg; CA-20mg/kg; Sham and Control.

**Materials and Methods:** Cell proliferation was evaluated by MTS assay in primary and T-HESC cell cultures. Mice received the compounds daily by intraperitoneal injection from post-surgical day 14 and continued until day 28. After treatment, animals were sacrificed, the abdomen was opened, lesions were counted, measured and their volume calculated.

**Results:** Wogonin 40, 80 and 160  $\mu$ M; CA 10, 12.5 and 25  $\mu$ g/ml and RA 25, 50 and 100  $\mu$ g/ml significantly inhibited cell proliferation in T-HESC cell line ( $p < 0.001$ ,  $p < 0.05$  and  $p < 0.05$  for Wogonin, CA and RA respectively). In addition, VD3 0.1, 0.5 and 1  $\mu$ M caused a similar effect ( $p < 0.001$ ). All these compounds inhibited cell proliferation in human eutopic endometrial stromal primary cultures ( $p < 0.05$ ,  $p < 0.01$  and  $p < 0.01$  for Wogonin, RA and VD3 respectively). Furthermore, the doses tested of CA and RA reduced the mean volume of established lesions in surgically induced endometriosis in mice ( $p < 0.05$  vs. Control). However, the number of established lesions did not differ from those of the Control group. No evidence of toxicity was noted in mice at the doses administered.

**Conclusion:** Wogonin, 1 $\alpha$ ,25-dihydroxvitaminD3, Rosmarinic Acid and Carnosic Acid inhibited endometrial cell proliferation. These results were supported by an in vivo study and found that RA and CA exerted an inhibitory effect on endometriosis development. The present findings are promising and support further investigation of these compounds as new therapeutics for endometriosis.

**Keywords:** Wogonin; Rosemary; 1 $\alpha$ ,25-dihydroxvitaminD3

Poster - Complementary therapies

P-10

**COMPARISON ON BMD CHANGES ACCORDING TO KINDS OF GNRH AGONIST FOR POSTOPERATIVE HORMONE THERAPY OF ENDOMETRIOSIS**

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**Objectives:** to compare the clinical characteristics, changes of bone mass density among gonadotropin-releasing hormones (leuprolide (Leuprin), triptorelin (Decapeptyl) and goserelin (Zoladex)) for postoperative hormonal therapy of endometriosis.

**Design:** This study was a retrospective medical record review of patients

**Materials and Methods:** For each group, thirty women were subjected to use 6 times GnRH agonists for postoperative treatment of endometriosis from January 1998 through December 2006 in Kangnam St Mary's hospital. All patients had add-back therapy by using estrogen plus progesterone, tibolone, alendronate.

**Results:** The FSH measured after 6 times of goserelin use was lower than those of leuprolide and triptorelin ( $p < 0.01$ ). The estradiol measured after 6 times of leuprolide use was higher than those of triptorelin and goserelin ( $p = 0.04$ ). The proportion of patients whose value of estradiol were checked less than 30pg/ml were 40% from leuprolide, 56% from triptorelin and 91% from goserelin.

**Conclusion:** Among GnRH agonist for postoperative hormone therapy of endometriosis, no statistically significant change on BMD were appeared. But, when we compared the potential bone protective effect by estradiol level, leuprolide could be considered the most effective and conservative choice.

**Keywords:** endometriosis, GnRH, BMD

## Poster - Complementary therapies

P-11

### LIVING LIFE TO THE FULLEST: IMPROVING QUALITY OF LIFE IN ENDOMETRIOSIS PATIENTS WITH PELVIC PHYSICAL THERAPY

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**Objectives:** Endometriosis impacts quality of life and general welfare of its sufferers. Even after surgical and medical intervention some women may have persistent symptoms. A multidisciplinary approach including an evaluation of the pelvic floor musculature, myofascial components, and the central nervous system should be integrated to any endometriosis treatment plan.

**Design:** A critical retrospective analysis of 10 post surgical patients treated with Pelvic Physical Therapy. Choice of treatments with respect to symptoms, pathology, and outcome will be discussed.

**Materials and Methods:** Patient interview on subjective reporting of symptoms at the onset of pelvic physical therapy, at the 4 week mark and at the cessation of therapy.

**Results:** Patients indicated an improvement in quality of life throughout therapy and a decrease in their pain overall. Quality of life was improved in all areas from return to work to improved interpersonal relationships. The increase of quality of life was attributed to decreases in pain symptoms. Pain decreases were noted on VAS repeatedly throughout therapy.

**Conclusion:** Pelvic Physical Therapy is an important component to increasing quality of life with endometriosis and in decreasing complaints of pain.

**Keywords:** Pelvic Physical Therapy

## Poster - Diagnosis and Screening

P-12

### ANALYSIS OF SPONTANEOUS ENDOMETRIOSIS IN CYNOMOLGUS MONKEYS (MACACA FASCICULARIS) BY LAPAROSCOPY AND MRI

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**Objectives:** Endometriosis is only found in primates, such as baboons, rhesus monkeys, and cynomolgus monkeys, but it is not clear whether the character of their disease state is similar to that in human. This study aims to clarify the disease state and determine the progression of spontaneous endometriosis in cynomolgus.

**Design:** We selected 18 female cynomolgus by their clinical symptoms (aberrance in palpation, CA125 and ultrasonographic examination, etc) in Tsukuba Primate Research Center, Japan. Ten of the 18 monkeys were diagnosed definitively with endometriosis by laparoscopy, and were monitored for food intake and menstrual bleeding.

**Materials and Methods:** The 10 monkeys were monitored for clinical condition by laparoscopy and MRI. The state of endometriosis was evaluated by measuring the adhesion (location and extension) and lesion (location and size) twice by laparoscopy and the cyst volume by MRI more than twice.

**Results:** The disease state of spontaneous endometriosis at diagnosis varied from mild to severe and had typical lesions, such as ovarian cysts and blueberry spots on the peritoneal wall, and adhesions at the ovary and Douglas' pouch. Adhesion at the vesicouterine pouch, possibly caused by their head forward posture, was a frequent site of adhesion specific to cynomolgus. Two monkeys had large ovarian cysts (measured as larger than 10 cm<sup>3</sup> by MRI) that compressed on other peritoneal organs inside the abdomen. From observation over a few months, endometriosis tended to progress or be stable. Food intake decreased in all 10 monkeys with endometriosis. In four monkeys whose food intake especially decreased during the menstrual phase, three of them had adhesions at the Douglas' pouch.

**Conclusion:** The pathology of endometriosis in cynomolgus was similar to that in human in terms of location and the various states, including severe. Because the disease states of spontaneous endometriosis in cynomolgus progressed over a few months, endometriosis in cynomolgus is useful for researching the etiology of the disease.

**Keywords:** Cynomolgus, MRI, Laparoscopy

## Poster - Diagnosis and Screening

P-13

### ULTRASOUND DIAGNOSIS OF UTEROSACRAL LIGAMENTS' ENDOMETRIOSIS : DESCRIPTION OF A NEW SIGN

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**Objectives:** Pelvic endometriosis is suspected by clinical examination but only confirmed by histology. Before surgery, transvaginal ultrasonography and magnetic resonance imaging are useful for lesions mapping. Uterosacral ligaments are affected in 69% of patients with deep infiltrating endometriosis. We propose a new ultrasound sign to detect the infiltration of uterosacral ligaments.

**Design:** In this prospective observational study, we examined preoperative ultrasound images digitally archived without knowing operative results, looking for a new sign of uterosacral ligament's endometriosis. Presence or absence of the sign was compared to the presence of a deep infiltrating endometriosis involving uterosacral ligaments at surgery and histology.

**Materials and Methods:** Patients were explored by the same sonographer. The sign corresponds to a distortion of the natural curvature of the endocervix-endometrial junction, resulting from attractions due to uterine adhesions caused by endometriosis. The sign is not present if there is continuity of the junction on a strict sagittal uterine axis.

**Results:** 52 patients were included during the study period. All patients were explored for pelvic chronic pain. We identified the sign for 37 of 52 patients by analysing ultrasound images. At surgery, uterosacral ligaments' endometriosis was found for 38 of 52 patients. The sensitivity of this new sign in our population was 81% (95% CI : 65-92), and the specificity 57% (95% CI : 29-82), with a C-index of 0.69 (95% CI : 0.54-0.84).

**Conclusion:** We propose a new ultrasound sign of uterosacral ligaments' endometriosis, useful for preoperative mapping. Nonetheless, we studied the new sign on pictures while we should appreciate this sign during the examination, taking advantage of dynamic character of ultrasound exam.

**Keywords:** Endometriosis, Uterosacral ligaments

## Oral

P-14

### COMMUNICATING ENDOMETRIOSIS WITH YOUNG WOMEN TO DECREASE DIAGNOSIS TIME

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**Objectives:** Communicating endometriosis to young women for early diagnosis and timely treatment could be important for long term disease outcomes. Our objective was to determine what young women know about endometriosis, what young women want to know about endometriosis and how this is best communicated to promote early detection.

**Design:** Focus group and population based online survey of young women aged 16-25 years.

**Materials and Methods:** A pilot focus group was conducted to trial questions. A population-based sample (N=131) completed a short online survey advertised through schools, a university and social media. The survey asked what they wanted to know about endometriosis, who should be targeted, mediums for obtaining information and who they would discuss with.

**Results:** 51% of participants had heard of endometriosis with a greater proportion being older participants; 89% thought teenagers should know about endometriosis with 78% agreeing that young men should also be aware; school was the most popular nominated source for viewing/discussing endometriosis information (40%) followed by the internet (22%) and magazines (13%). Young women were more comfortable talking to a doctor (75%) about endometriosis, followed by a parent (59%) or friend (51%). Participants wanted to know identifying symptoms, the disease definition, commonality, risk factors, causes, prevention, treatment and diagnosis. Participant's descriptions of the disease were vague and sometimes confused.

**Conclusion:** In this study, most young women want to learn about endometriosis, think that young men should also be educated, and are most likely to access information through school based programs and the internet. For early education regarding endometriosis, health promotion activities should be directed towards sources that young women prefer.

**Keywords:** Communication, endometriosis, youth

## Poster - Diagnosis and Screening

P-15

### A NOVEL NONINVASIVE TECHNIQUE USING TRANSVAGINAL SONOGRAPHY AFTER BOWEL PREPARATION (TVSBP) FOR URETERAL EVALUATION IN WOMEN UNDERGOING PELVIC MAPPING OF DEEPLY INFILTRATING ENDOMETRIOSIS (DIE)

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**Objectives:** To describe a novel and easy noninvasive pre-and-postoperative technique using TVSBP for ureteral evaluation in women with DIE

**Design:** Prospective observational study during the interval of 06/10 to 06/13 evaluating 1674 TVSBP performed in 1483 women for DIE mapping.

**Materials and Methods:** Patients drank 300 mL of water before exam. Pelvic ureter segments imaging required fifteen minutes from the initiation of scanning. Antegraded/retrograded axial plane scanning from uretero-vesical junction to the iliac vessels to identify wall infiltration and measuring the distance to contiguous DIE. Surgery and histology findings were used for confirmation.

**Results:** At least one ureter was identified in all women and in 95%, both ureters were seen. Urinary jet stream from both ureters into the bladder can easily observed using power Doppler. Seven extrinsic ureteral DIE lesions were distributed among retrocervical, paracervical and ovarian fossae. There was an excellent association between the ultrasound and surgical findings in all women who presented with ureteral endometriosis. Further, there was a very good parallel in measuring the distance of retrocervical and paracervical nodules with the ureteral pathway.

**Conclusion:** Pelvic segments of the ureters can be easily identified, ureteral peristalsis appreciated and jet stream flow from the ureters into the bladder appreciated using ultrasound scanning with power Doppler function. Furthermore, this novel technique is an easy, noninvasive way to evaluate the pelvic ureters without the need of contrast material.

**Keywords:** Ureter, endometriosis, ultrasonography

## Poster - Diagnosis and Screening

P-16

### PREVALENCE OF PRE-OPERATIVE URODYNAMIC ABNORMALITIES IN WOMEN WITH DEEP INFILTRATING ENDOMETRIOSIS: A DESCRIPTIVE STUDY.

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**Objectives:** Post-operative transient urinary problems usually occur after large bowel resections. Sometimes, when problems last longer than few days, the contribution of some pre-operative conditions may be suspected. We aim to describe (pre-operatively) the prevalence of the main urinary symptoms and urodynamic findings in women with deep infiltrating endometriosis (DIE).

**Design:** Cross-sectional (pre-planned) observational study (Canadian Task Force Classification II-2) including a total of 70 women aging 15-56y who were, during diagnostic routine, evaluated before undergoing laparoscopic cytoreductive surgery (June/2011-August/2013). The diagnosis of DIE (infiltration>5mm) was considered with basis on clinical features and nuclear-magnetic-resonance-imaging (interpreted by an experienced radiologist).

**Materials and Methods:** Assessed urinary symptoms: urgency, perception of bladder fullness, incontinence, diurnal micturition, nocturia, dysuria/strangury, interrupted urine flow, Valsalva maneuver and feeling of incomplete urination. Urodynamic variables: maximum flow, post-voiding residue, sensitivity, complacency, maximum cystometric capacity (MCC), opening pressure, maximum pressure in urination, detrusor contractility (Schäffer's nomogram) and obstruction (Abrams-Griffiths's nomogram).

**Results:** Posterior-compartment had some DIE-lesion in 96% of women (70% showed lesions in sigmoid-colon); anterior-compartment was affected in 41% of patients. Prevalence of symptoms (descending order): at least one symptom (34.8%), necessity of high abdominal pressure for micturition (27.5%), incontinence (21.7%), urgency (20.3%), feeling of incomplete urination (14.5%), interrupting voiding (10.1%), recurrent urinary infection (10.1%), dysuria (7.2%) and hematuria (1.4%). Prevalence of urodynamic findings (descending order): maximum flow  $\leq 15$  mL/sec (56.5%), open pressure  $\geq 30$  cmH<sub>2</sub>O (50.0%), obstruction/Abrams-Griffiths's nomogram (23.5%), complacency  $\leq 20$  mL/cmH<sub>2</sub>O (20.3%), decrease sensibility (18.7%), high post-micturition volume/ $\geq 15$ % of MCC (17.4%), low detrusor pressure in maximum urination (10.3%), detrusor hyperactivity (8.8%), high sensibility (7.2%), detrusor contractility/Schäffer's nomogram (5.8%) and low MCC/ $\leq 350$  mL (4.3%).

**Conclusion:** Considering women in whom several sites were affected by DIE, data suggested that urinary symptoms or urodynamic findings might exist before surgery in more than 1/3 of the patients. Mild obstructive findings detected by urodynamic testing seem to be less perceived by patients and, probably, sub estimated in most cases.

**Keywords:** Urodynamic, voiding, diagnostic.

## Poster - Diagnosis and Screening

P-17

### MODELING THE RISK OF ENDOMETRIOSIS USING ENSEMBLE-BASED PREDICTION MODELS

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**Objectives:** A diagnosis of endometriosis is generally achieved by invasive surgery and depends on the surgeons' clinical expertise. Accurate predictive models for endometriosis, which may rule out unnecessary invasive surgeries, are few. Moreover, there is a gap in the literature in approaches for modeling endometriosis risk in ethnically diverse populations.

**Design:** Cross-sectional study of existing patient registry data.

**Materials and Methods:** We aimed to develop a predictive model for endometriosis using Patient Registry data (Endometriosis Research Program, PSMHS). After data pre-processing and consolidating the variables, we compared traditional logistic regression approaches to the more novel tree-based ensemble prediction models (random forest, gradient boosted trees, conditional inference trees) for endometriosis risk estimation.

**Results:** Ninety-nine potential predictors for endometriosis were considered. Artificial contrast ensemble (ACE) feature selection was used to reduce the dimensionality of the problem. Only 27 predictors were found to successfully discriminate ( $\alpha=0.01$ ) between women with a surgical diagnosis of endometriosis and women without the disease and/or without a surgical diagnosis. For logistic regression, the model was simplified further by performing cross-validation and maintaining only predictors that were statistically significant ( $\alpha=0.05$ ) in more than two of the models fitted with the cross-validation training folds. This simplification led to an eleven-predictor model with a performance comparable to all models fitted with 27 predictors. Further ensemble models were used to assess the risk of severe vs. mild endometriosis in endometriosis patients.

**Conclusion:** This model offers a valuable tool that can be used in the clinical setting to evaluate a patient presenting with symptoms characteristic of endometriosis. It can be translated into a standardized online questionnaire that can be completed during a visit and used to determine whether patients may benefit from surgery.

**Keywords:** Endometriosis, prediction\_models, risk\_assessment

## Poster - Diagnosis and Screening

P-18

### WHAT ARE WE MISSING: THE ROLE OF EXPERT TRANSVAGINAL ULTRASOUND IN THE DIAGNOSIS AND MANAGEMENT OF ENDOMETRIOSIS

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**Objectives:** To determine if expert transvaginal ultrasound offers benefit over a routine transvaginal ultrasound in the diagnosis of endometriosis

**Design:** A retrospective chart review performed at a Canadian tertiary centre specializing in diagnosis and management of endometriosis.

**Materials and Methods:** All cases with surgically confirmed endometriosis and an expert directed endometriosis ultrasound completed at our centre were included for review. Findings from the expert ultrasound were compared to routine pelvic ultrasound performed for the same indication.

**Results:** A total of 40 cases were included. The sensitivity for diagnosis of endometriosis with expert transvaginal ultrasound was 77.5% (31/40) compared to 25.0% (10/40) with routine transvaginal ultrasound. Routine ultrasound diagnosis was based exclusively on the presence of endometrioma (10/10), with features other than endometrioma described only in two cases (2/10). Expert scan provided a detailed compartmentalized description of the extent of disease. Features of deep involvement were present in 96.7% (30/31) of cases with only one case diagnosed exclusively by presence of endometrioma. Posterior compartment was most commonly involved (90.3%) whereas anterior compartment was involved only in 19.3%. Routine ultrasound had a false negative rate of 70.8% (17/24), as features of endometriosis were picked up by expert scan in these cases.

**Conclusion:** Expert transvaginal ultrasound is highly sensitive in the diagnosis of endometriosis. Routine ultrasound fails to identify lesions other than endometriomas. Expert ultrasound provides an accurate and detailed compartmentalized approach, and may help in surgical planning.

**Keywords:** Diagnosis, Endometriosis, Imaging

## Poster - Diagnosis and Screening

P-19

### CAN WE USE THE SOFT MARKER, SITE-SPECIFIC TENDERNESS AT TVS, IN THE PRE-OPERATIVE MAPPING OF PERITONEAL ENDOMETRIOSIS?

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**Objectives:** To determine whether the presence of site-specific tenderness during TVS corresponds with the location of peritoneal endometriosis at surgery for women with suspected endometriosis.

**Design:** Multi-centre prospective observational study over 4 years. All women were of reproductive age, clinically suspect of endometriosis with a plan for laparoscopic surgery. A detailed pre-operative TVS was performed prior to surgery. Site-specific tenderness was elicited with the TV probe against each of six pelvic locations.

**Materials and Methods:** Women rated their pain score from 0 (no pain) to 10 (worst pain) for each of six locations. anterior fornix, right adnexa, left adnexa, right uterosacral ligament (USL), left USL and posterior fornix. Those with an endometrioma and/or posterior compartment deep infiltrating endometriosis at laparoscopy were excluded from the analysis.

**Results:** 189 consecutive women with TVS and laparoscopic outcomes were included in the final analysis. 100 women were found to have isolated peritoneal endometriosis. Peritoneal endometriosis was present in the following locations at surgery: left USL (39%), right USL (33%), left pelvic sidewall (30%), right pelvic sidewall (23%), pouch of Douglas (POD) (22%), uterovesical pouch (14%), left pararectal space (9%), right pararectal space (6%), and posterior cervix (4%). The only positive association between site-specific tenderness at TVS and peritoneal endometriosis location at surgery was for site-specific tenderness at the posterior vaginal fornix and the presence of peritoneal endometriosis in the POD (p=0.0486)

**Conclusion:** The use of site specific tenderness during TVS appears to be useful in the mapping of peritoneal endometriosis involving the POD.

**Keywords:** superficial endometriosis, POD

## Poster - Diagnosis and Screening

P-20

### THE ROLE OF TRANSVAGINAL ULTRASOUND WITH BOWEL PREP FOR DEEP ENDOMETRIOSIS IN THE TREATMENT ALGORITHM OF PATIENTS WITH CHRONIC PELVIC PAIN AND ENDOMETRIOSIS

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**Objectives:** To evaluate how transvaginal ultrasound with bowel prep (TVUS-BP) for deep endometriosis affects the treatment algorithm of patients with chronic pelvic pain and endometriosis.

**Design:** Our design is a retrospective chart review.

**Materials and Methods:** We evaluated forty patients who underwent a TVUS-BP for deep endometriosis between May 2012 and September 2013 at Mayo Clinic in Arizona. We reviewed data related to age, pain symptoms and specific sites of disease involvement on TVUS-BP. The management and treatment of these patients were then compared and evaluated.

**Results:** The mean age of the patients was 36.2 +/- 9. The most common symptoms were dysmenorrhea (24/40), chronic pelvic pain (24/40), and dyspareunia (18/40). Fifteen patients had positive findings on the TVUS-BP. Of these, eleven underwent laparoscopy. TVUS-BP correlated with laparoscopic findings for rectosigmoid lesions in 2/2 patients, ovarian lesions in 4/5 patients, and rectocervical lesions in 2/4 patients. Twenty-five patients had negative findings on the TVUS-BP. Of these, twenty were managed conservatively (observation, ovarian suppression and/or physical therapy) with resolution of symptoms in the mean follow up time of 2.5 +/- 2.3 months. The other five patients underwent laparoscopy due to their pain. Three of the five had peritoneal endometriosis, which was not detectable on ultrasound and ultimately underwent ovarian suppression with symptom relief.

**Conclusion:** Transvaginal ultrasound with bowel prep for deep endometriosis is a feasible technique to evaluate patients with chronic pelvic pain. Our preliminary results suggest this can be incorporated into the treatment algorithm of patients with endometriosis and chronic pelvic pain, avoiding unnecessary surgery.

**Keywords:** Pelvic ultrasound, endometriosis

## Poster - Diagnosis and Screening

P-21

### INFLUENCE OF ENDOMETRIOSIS IN ANTERIOR-COMPARTMENT ON PREOPERATIVE URINARY ABNORMALITIES IN WOMEN WITH ENDOMETRIOSIS IN POSTERIOR-COMPARTMENT.

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**Objectives:** Considering only women who were affected by deep infiltrative endometriosis (DIE) in the posterior-compartment, we aim to assess the association between the occurrence of preoperative urinary abnormalities (specific urinary symptoms and urodynamic findings) and the presence of DIE also in the anterior-compartment.

**Design:** Cross-sectional (pre-planned) observational study (Canadian Task Force Classification II-2) including a total of 50 women (aging 15.8 to 52.8y) who were evaluated before undergoing laparoscopy for DIE during preoperative diagnostic routine from June/2011-August/2013.

**Materials and Methods:** Preoperative diagnosis of DIE was suspected with basis on clinical features and ensured by an experienced radiologist with basis on nuclear magnetic resonance imaging. Anterior-compartment included bladder, anterior cul-de-sac, anterior broad-ligament, anterior uterine serosa and round-ligaments. Associations between dichotomized variables were assessed through nonparametric Fisher's Exact Test (2-sided).

**Results:** The prevalence of DIE-lesion in the anterior-compartment in this sample of women with DIE and posterior-compartment was 38.5% (95%CI: 25.5-52.0%) whereas the prevalence of urinary symptoms was 34.0% (95%CI: 20.7-47.2%). Considering the main urinary symptoms (urgency, perception of bladder fullness, incontinence, diurnal micturition, nocturia, dysuria/strangury, interrupted urine flow, Valsalva maneuver and feeling of incomplete urination) and the main urodynamic variables (maximum flow, post-voiding residue, sensitivity, complacency, maximum cystometric capacity, opening pressure, maximum detrusor pressure, detrusor contractility according Schäffer's nomogram and obstruction according Abrams-Griffiths's nomogram), there was no significant association between DIE-lesion in the anterior-compartment and any urinary symptoms or any variable assessed during urodynamic testing.

**Conclusion:** Our preliminary findings suggest that preoperative urinary abnormalities are independent of presence of endometriosis in the anterior-compartment when women are affected by DIE in posterior-compartment.

Actually, data didn't allow exclude the probability of preoperative urinary abnormalities be linked to any pelvic structures.

**Keywords:** Urodynamic, endometriosis, voiding.

## Poster - Diagnosis and Screening

P-22

### THE PREDICTION OF POD OBLITERATION USING OFF LINE ANALYSIS OF THE REAL TIME DYNAMIC SLIDING SIGN BY INDIVIDUALS WITH DIFFERENT LEVELS OF ULTRASOUND EXPERIENCE

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**Objectives:** To evaluate the performance of observers with different levels of ultrasound experience in predicting POD obliteration using off line analysis of the real time dynamic sliding sign.

**Design:** 26 pre-recorded video sets of women presenting with chronic pelvic pain were viewed offline by six observers with varying ultrasound experience in order to predict POD obliteration using the real time dynamic 'sliding sign' technique. All 26 women had laparoscopic confirmation of POD status.

**Materials and Methods:** Observers 1 – 6 had each performed 0, 50, 200, 50, 750 and 15000 scans respectively. Each observer viewed the videos in two anatomic locations (retro-cervix and posterior uterine fundus) to determine POD obliteration. The diagnostic performance and inter-observer correlation were determined by comparing observers against gold standard laparoscopy.

**Results:** There was substantial agreement among observers in the prediction of an obliterated POD (Cohen's coefficient 0.613) using the real time dynamic sliding sign. The diagnostic performance for the prediction of POD obliteration by the observers (1, 2, 3, 4, 5) were 65.4%, 84.6%, 84.6%, 80.8%, 96.2%, respectively when compared with gold standard laparoscopy.

**Conclusion:** Minimal transvaginal ultrasound experience is required to predict POD obliteration.

**Keywords:** transvaginal ultrasound, POD

## Poster - Diagnosis and Screening

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### MUFEC (MRI ULTRASOUND FUSION FOR ENDOMETRIOSIS CHARACTERIZATION)

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**Objectives:** To combine complementary information from MRI and TVUS (trans-vaginal ultrasound) images of rectovaginal endometriotic nodule, to locate the US intersecting plane in the MRI volume, and to quantify the deformability of endometrial tissue and surrounding structure.

**Design:** We used two models. Clinical model: TVUS and MRI images (10 patients). Semi-automatic model: original data were deformed using a biomechanical model to simulate physical deformation. A segmentation (delimitation) of the nodule was performed in the two modalities (MRI and TVUS) and recent mathematical approaches in shape analysis were applied.

**Materials and Methods:** We developed a new mathematical method to combine TVUS and MRI images: MUFEC (MRI Ultrasound Fusion for Endometriosis Characterization). Joint registration and deformation quantification of endometrial tissue using MRI and TVUS measurements were studied

**Results:** Our approaches provide optimal curves on MRI surfaces that match with the original TVUS curves. This study results in an accurate quantification and localization of the deformable endometriotic tissue. Using both semi-automatic simulated data and original real data from ten patients, we were able to visually improve the preoperative diagnosis by facilitating interpretation of ultrasound data. Combining image from MRI and TVUS allows to compensate differences in patient positioning during MRI and TVUS observations, and the potential deformation of endometrial tissue during TVUS measurement process (pressure on the probe).

**Conclusion:** These results could improve planning of surgical procedures. We believe that combining complementary information from both modalities, locating the US plane inside the MRI volume, and quantifying deformability of endometriosis under a given level of applied stress can open new avenues for diagnosing and monitoring complex cases.

**Keywords:** Segmentation, endometriosis, fusion

## Poster - Diagnosis and Screening

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### THE SIGNIFICANCE OF SYMPTOM AND PHYSICAL SIGN TO DIAGNOSIS OF DEEPLY INFILTRATING ENDOMETRIOSIS

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**Objectives:** To study the significance of pain symptom and physical sign to diagnosis of deeply infiltrating endometriosis (DIE)

**Design:** This study was designed as retrospective and control clinical study

**Materials and Methods:** 500 patients with laparoscopic diagnosis of endometriosis were studied retrospectively and divided into two groups depending on the existence of the deeply infiltrating endometriosis. The pain symptoms and gynecological physical signs were recorded detail, and the correlation with diagnose of DIE were analyzed

**Results:** (1) The significance of pain symptoms: the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and OR(95%CI) of each pain symptom were: dysmenorrhoe (90.5%, 37.%, 59.6%, 79.3% , 5.66 (3.46-9.28) ), chronic pelvic pain (35.2%, 82.6%, 67.4%, 55.4%, 2.58 (1.70-3.91) ), dyspareunia (46.2%, 80.6%, 70.7%, 59.6%, 3.56 (2.39-5.32) ), dyschezia (51.0%, 73.7%, 66.5%, 59.5%, 2.91 (2.00-4.21) ), respectively. (2) Pelvic physical examination. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of each pain symptom were: fixed uterine:73.6%, 71.2%, 79.5%, 64.0% ; fixed ovarian cyst:94.1%, 20.3%, 63.3%, 70.0% ; uterosacral ligaments nodule : 47.1%, 97.5%, 96.6%, 54.9% ; uterosacral ligaments nodule with tenderness : 81.7%, 75.0%, 83.1%, 73.2%, 13.36 (6.73-26.52); rectovaginal septum nodule : 32.2%, 100%, 100%, 49.4%, rectovaginal septum nodule with tenderness : 32.2%, 100%, 100%, 49.4% ; blue nodule in posterior vaginal fornix : 14.9%, 100%, 100%, 43.7%.

**Conclusion:** Dysmenorrhoe has the highest sensitivity and NPV, CPP has the highest specificity, and dyspareunia has the highest PPV for the diagnosis. Nodule on uterosacral ligament, rectovaginal septum with tenderness, the blue lesion on posterior fornix also has strong significance. Symptom and vaginal examination could improve the diagnosis DIE obviously before procedure.

**Keywords:** Diagnosis, pain, physical-sign

## Poster - Diagnosis and Screening

P-25

### DYSFUNCTIONAL VOIDING AND URODYNAMIC CHANGES IN WOMEN WITH BLADDER ENDOMETRIOSIS.

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**Objectives:** Since urinary abnormalities are not always exactly the same for every woman affected by deep infiltrating endometriosis (DIE), we aim to verify the association of major urinary symptoms and of urodynamic findings with the presence of endometriosis in the bladder, a major structure involved with the micturition.

**Design:** Cross-sectional (pre-planned) observational study (Canadian Task Force Classification II-2) including a total of 54 women (aging 15.8 to 52.8y) who were evaluated before undergoing laparoscopy for DIE during preoperative diagnostic routine from June/2011 to August/2013 in Rio de Janeiro, Brazil.

**Materials and Methods:** Preoperative diagnosis of DIE was suspected with basis on clinical features and ensured by an experienced radiologist with basis on nuclear magnetic resonance imaging. The associations between dichotomized variables were assessed with the nonparametric Fisher's Exact Test (2-sided).

**Results:** The prevalence (95% confidence interval) of DIE-lesion in the bladder was 16.7% (95%CI: 7.4-27.8%) whereas the prevalence of urinary symptoms was 34.8% (95%CI: 24.6-46.4%); there was no significant association between DIE-lesion in the bladder and urinary symptoms ( $p=.965$ ). However, presence of DIE-lesion in the bladder was statistically associated with maximum detrusor pressure  $<30\text{cmH}_2\text{O}$  (OR=10.5; 95%CI:1.4-76.3;  $p=.03$ ), an asymptomatic variable that reflects bladder hypo contractility.

**Conclusion:** Our preliminary findings suggest that preoperative urinary symptoms are independent of presence of endometriosis in the bladder when women are diffusely affected by DIE. Actually, we couldn't exclude the probability of preoperative urinary abnormalities be linked to other pelvic structures because this sample didn't include only cases with bladder endometriosis.

**Keywords:** Urodynamic, bladder, voiding.

## Poster - Diagnosis and Screening

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### ULTRASONOGRAPHY WITH BOWEL PREPARATION IS A USEFUL TOOL FOR DIAGNOSIS OF APPENDIX , ILEUM AND CECUM ENDOMETRIOSIS

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**Objectives:** Endometriosis compromising the appendix, ileum and cecum corresponds about 15% of patients with bowel endometriosis. To determine the involvement of these intestinal segments and the efficacy of ultrasound with bowel preparation for the pre-operative diagnosis of disease considering these specific sites.

**Design:** A prospective study of patients with clinically suspected endometriosis were submitted to pelvic and transvaginal ultrasound (PUS-BP and TVUS-BP). Sonographic findings from the right iliac fossa were compared with the surgical anatomic findings. All specimens were submitted to histological confirmation of endometriosis. Sensitivity, specificity and likelihood ratio were calculated.

**Materials and Methods:** Between May 2008 and September 2013, 524 consecutive patients underwent laparoscopy. Prior to surgery, ultrasound findings of size, number and location of lesions in the right iliac fossa (RIF) were recorded.

**Results:** We found 268 lesions of endometriosis in rectosigmoid and 55 affecting the RIF. Specifically, 38 (69.1%) lesions affecting the appendix, 9 (16.4%) in the ileum and 8 (14.5%) in the cecum. All patients with endometriosis in the right iliac fossa had at least one concomitant lesion in other site, confirming the multifocal aspect of endometriosis. PUS-BP with TVUS-BP showed sensitivity and specificity, respectively as follows: 86.7% and 100% for appendix; 81.8% and 100% for ileum and 100% and 100% for cecum. Overall, considering this imaging exams for the diagnosis of endometriosis involving the appendix, ileum and cecum, we found a sensitivity of 86.9%, specificity of 100%, positive likelihood ratio ( LR +) --- and negative likelihood ratio ( LR - ) 0.13.

**Conclusion:** These findings demonstrated that ultrasound is an adequate imaging exam for the pre-operative diagnosis of endometriosis in the appendix, ileum and cecum confirming the usability of this method.

**Keywords:** Endometriosis, ultrasonography, diagnosis

## Poster - Diagnosis and Screening

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### IS SITE-SPECIFIC TENDERNESS AT TRANSVAGINAL SCAN (TVS) ASSOCIATED WITH POUCH OF DOUGLAS OBLITERATION AT LAPAROSCOPY IN WOMEN WITH SUSPECTED ENDOMETRIOSIS?

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**Objectives:** To determine whether there is an association between pouch of Douglas (POD) obliteration at laparoscopy and site specific tenderness during Transvaginal scan.

**Design:** Multi-centre prospective observational study over 4 years. All women were of reproductive age, clinically suspect of endometriosis with a plan for laparoscopic surgery. A detailed history and pre-operative TVS was performed prior to surgery. Site-specific tenderness was elicited with the TV probe against each of the six pelvic locations.

**Materials and Methods:** Women rated their Visual Analogue Score (VAS) for each of the six locations. All women underwent laparoscopy +/- excision of endometriosis and determination of POD obliteration at surgery was made. The relationship between site-specific tenderness at TVS and POD obliteration at laparoscopy were analyzed for significance.

**Results:** 189 women were included in this study. 47/189 (25%) had POD obliteration at laparoscopy. Of the six pelvic locations assessed at TVS (namely anterior fornix, right adnexa, left adnexa, right uterosacral ligament, left uterosacral ligament and posterior fornix) for site-specific tenderness, none was significantly associated with POD obliteration at laparoscopy.

**Conclusion:** This study found that site-specific tenderness during TVS does not seem to be useful in the prediction of POD obliteration at laparoscopy.

**Keywords:** Pod, vas

## Poster - Diagnosis and Screening

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### WHAT IS THE VALUE OF COLONOSCOPY IN THE DIAGNOSIS OF BOWEL ENDOMETRIOSIS?

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**Objectives:** Bowel involvement, which affects 5-30% of women with endometriosis, causes a variety of symptoms mimicking inflammatory conditions, IBS, or malignancy. As endometriosis rarely involves the mucosa, colonoscopy has been thought to be of limited value. This study evaluates the role and outcomes of colonoscopy amongst women requiring segmental bowel resection.

**Design:** Prospective case series of all women who underwent laparoscopic segmental bowel resection for treatment of endometriosis at a university-affiliated tertiary referral centre between March 2003 and April 2012 by a single gynecologist and 4 colorectal surgeons.

**Materials and Methods:** Information was obtained from a prospectively maintained database, including patient demographics, history, presenting symptoms, diagnostic evaluation, and operative and histopathologic findings. The location of bowel involved was defined by the level of resection: high (>10cm from anal verge), low (6-10cm), ultra-low (<6cm) and ileo-caecal.

**Results:** 73 patients had 29 ultralow, 24 low, 17 high, and 4 ileocaecal resections. Only 1 (1.4%) had mucosal involvement on final histopathology. Abdominal pain was the most common presenting symptom; however, dyschezia (75.5% vs. 50.0%,  $P=0.037$ ), and hematochezia (34.0% vs. 10.0%,  $P=0.040$ ) were more commonly associated with low and ultralow lesions. Patients with low and ultralow disease were more likely to have an immobile uterus on examination (67.3% vs. 20.0%,  $P=0.001$ ). 37 (50.7%) patients underwent a colonoscopy under the discretion of the colorectal surgeon, based on presence of hematochezia and/or family history of colon cancer ( $P<0.001$ ); 21 (56.8%) were found to have either an extramucosal mass, or an extrinsic stricture – not significantly different between the low/ultralow and high/ileocaecal groups (52.0% vs. 75.0%,  $P=0.184$ ).

**Conclusion:** Management of bowel endometriosis requires a multidisciplinary team. This study supports the continuing role and value of colonoscopy in the preoperative assessment of bowel involvement and exclusion of incidental bowel pathology in women with symptoms suggestive of infiltrating bowel endometriosis.

**Keywords:** Bowel resection, colonoscopy

## Poster - Diagnosis and Screening

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### IS EXPERIENCE RELEVANT WHEN EVALUATING THE POUCH OF DOUGLAS (POD) USING THE REAL TIME DYNAMIC SLIDING SIGN? - AN INTER OBSERVATIONAL STUDY.

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**Objectives:** To determine the level of transvaginal ultrasound (TVS) experience required to evaluate the POD using the real time dynamic sliding sign.

**Design:** Prospective observational study. 32 pre-recorded TVS “sliding sign” video sets were viewed offline by six observers (1 - 6) with varying ultrasound experience. Observers 1 – 6 had each performed 0, 50, 200, 50, 750 and 15000 scans respectively. Observer 6 was the gold standard for comparison.

**Materials and Methods:** Each observer viewed the videos in two anatomic locations (retro-cervix and posterior uterine fundus) and determined if the sliding sign was positive or negative at each location. The observers were asked to reanalyse the same videos in a different order, at least 7 days later to assess for intra-observer agreement.

**Results:** An analysis of the inter-observer correlation was performed using the Cohen's coefficient to evaluate the degree of inter observer agreement. The overall agreements between observers for the accurate interpretation of the real time dynamic sliding sign was moderate with a Fleiss' kappa 0.499 (95% CI 0.458 - 0.541). However, the pairwise rater agreement demonstrated significant to near perfect agreement for those observers that have performed 200 or more transvaginal scans (Cohen kappa 0.712 - 0.891).

**Conclusion:** In our study, if the observer has performed at least 200 TVS, there is substantial to almost perfect agreement with the expert when interpreting the sliding sign

**Keywords:** sliding sign, POD

## Poster - Diagnosis and Screening

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### INTRA OBSERVER VARIABILITY IN THE INTERPRETATION OF THE REAL TIME DYNAMIC SLIDING SIGN

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**Objectives:** To evaluate the intra observer variability in the interpretation of the real time dynamic sliding sign.

**Design:** Prospective observational study. 32 pre-recorded TVS “sliding sign” videos in 2 sets were viewed offline by six observers (1 - 6) with varying ultrasound experience. Observers 1 – 6 each performed 0, 50, 200, 50, 750 and 15000 scans respectively. Observer 6 was the gold standard for comparison

**Materials and Methods:** Each observer viewed the videos in two anatomic locations (retro-cervix and posterior uterine fundus) and determined if the sliding sign was positive or negative at each location. The same observer also reanalysed the same videos, albeit in a different order, at least 7 days later to assess for intra-observer agreement.

**Results:** An analysis of the intra-observer correlation was performed comparing observers 1-5 against observer 6 (the gold standard). Cohen's coefficient was used to evaluate the degree of intra observer agreement. Observers with 200 or more TVS experience had substantial to almost perfect intra observer agreement (Cohen coefficient 0.74 -0.91) compared to those with less ultrasound experience (Cohen coefficient 0.45 -0.50).

**Conclusion:** Intra - observer correlation was substantial to almost perfect if the observer had performed 200 or more pelvic scans.

**Keywords:** Ultrasound, sliding sign

Poster - Diagnosis and Screening

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**PROSPECTIVE EVALUATION OF A PANEL OF CYTOKINES AS POTENTIAL SERUM MARKERS OF PELVIC ENDOMETRIOSIS**

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**Objectives:** This study was designed to assess the diagnostic value of a panel of serum cytokines to detect endometriosis in women undergoing laparoscopy for gynecological complains.

**Design:** A prospective cohort study including 77 consecutive women scheduled for laparoscopy for chronic pelvic pain, infertility or ovarian cyst.

**Materials and Methods:** Preoperatively, we collected blood samples from a peripheral vein and measured serum interleukin (IL)-2, IL-4, IL-6, IL-10, interferon (INF)-gamma and tumor necrosis factor (TNF)-alpha concentrations by Cytometric Bead Array Flex Set System. Endometriosis was confirmed by histopathological examination of surgical specimens.

**Results:** IL-2, IL-4, IL-6, IL-10, INF-gamma and TNF-alpha concentrations were not able to distinguish the women who eventually were diagnosed with endometriosis. Patients with chronic pelvic pain had serum IL-6/IL-10 ratios significantly higher than patients without this condition, independently of the presence of endometriosis (6.8 +/- 0.6 vs. 4.7 +/- 0.4, p<0.05).

**Conclusion:** The present study demonstrated that IL-2, IL-4, IL-6, IL-10, INF-gamma and TNF-alpha do not predict endometriosis in a cohort of symptomatic women. The discovery of new biomarkers remains a priority in endometriosis research but we are far from achieving this goal.

**Keywords:** Endometriosis, cytokines, diagnosis.

## Poster - Diagnosis and Screening

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### IDENTIFICATION OF TWO POSSIBLE NEW BIOMARKERS USING ULTRA-DEEP MIRNA SEQUENCING IN ENDOMETRIOSIS PATIENTS.

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**Objectives:** Our aim was to found possible new biomarkers for endometriosis detection.

**Design:** Total RNA of cells originated from eutopic endometrium of stage IV endometriosis patients (09 samples), as well as, RNA of cells originated from endometrium of healthy women (07 samples) was extracted.

**Materials and Methods:** Product of RNA extraction was enriched for small RNAs and used for microRNA expression analysis on SOLiD4 sequencer. Sequences were mapped against the miRBase using CLC Genomics Workbench 6.0.1

**Results:** An average of 5 million reads per sample was mapped on known miRNAs. After mapping and normalization of reads, we used the program EdgeR to identify differently expressed miRNAs, those with  $p < 0.01$  and  $FDR < 0.05$ . With this methodology we could obtain two differentially expressed miRNAs between the samples, with high potential to be confirmed as biomarkers.

**Conclusion:** So, this approach is feasible for new biomarkers search.

**Keywords:** Endometriosis, biomarkers, miRNA

## Poster - Diagnosis and Screening

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### CALDESMON IS A POTENTIAL MARKER FOR ENDOMETRIOSIS

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**Objectives:** Considerable effort has been invested in searching for less-invasive methods of diagnosing endometriosis. The aims of our study were to investigate whether caldesmon protein levels are differentially altered in the endometrium and endometriotic lesions and to evaluate the performance of this protein as potential biomarkers for endometriosis.

**Design:** A case-control study was conducted on women with and without endometriosis in the proliferative and secretory phases of the menstrual cycle.

**Materials and Methods:** Paired biopsies of endometrial tissue and endometriotic lesions were obtained from patients with endometriosis to evaluate caldesmon protein levels by western blotting. It was performed caldesmon immunostaining for cellular localization. Endometrium from women without endometriosis was used as a control.

**Results:** Increased caldesmon levels were detected in the endometriotic lesions. The electrophoretic profile of caldesmon by western blotting was clearly different between the studied groups. Caldesmon expressed by the immunostaining showed no variation among the cell type of endometriotic lesions and eutopic endometrium. Stromal cells marked positively in eutopic endometrium from control patients and in the endometriosis lesions. The presence of caldesmon in the endometrium of patients with and without endometriosis permitted diagnoses with 95% sensitivity (specificity 100%) and 100% sensitivity (specificity 100%) for the disease and for minimal-mild endometriosis in the proliferative phase of the menstrual cycle, respectively. In the secretory phase, minimal-mild endometriosis was detected with 90% sensitivity and 93.3% specificity.

**Conclusion:** Caldesmon is a possible predictor of endometrial dysregulation in patients with endometriosis.

**Keywords:** Caldesmon; Endometriosis; Diagnosis.

## Poster - Diagnosis and Screening

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### PREDICTION OF POUCH OF DOUGLAS (POD) OBLITERATION USING THE REAL TIME DYNAMIC SLIDING SIGN - A REVIEW OF 200 CASES UNDERGOING LAPAROSCOPY

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**Objectives:** To evaluate the accuracy of the real time dynamic sliding sign in the prediction of POD obliteration – a review of 200 cases

**Design:** A prospective evaluation of 200 patients who had laparoscopic surgery for endometriosis over a 5-year period. All patients underwent a preoperative transvaginal ultrasound. All cases were compared with the gold standard laparoscopic POD findings.

**Materials and Methods:** The preoperative transvaginal ultrasound included an assessment of the POD using the real time dynamic sliding sign. At laparoscopy, the status of the POD was also recorded. Both the transvaginal ultrasound preoperative findings and the findings at laparoscopy were collated and analysed.

**Results:** The prediction of POD obliteration using the sliding sign was evaluated in the first 100 women and the performance of the test was compared to the second 100 women. The accuracy, sensitivity, specificity, PPV and NPV for predicting POD obliteration in the first 100 cases in our series was 94%, 83.9% 98.6%, 96.3% and 93.2% The accuracy, sensitivity, specificity, PPV and NPV for predicting POD obliteration in the later 100 cases in our series was 98%, 100% 97.5%, 90.9% and 100%

**Conclusion:** Since our first publication in 2012, the performance of our unit has improved when it comes to prediction of POD obliteration.

**Keywords:** Laparoscopy, sliding sign

## Poster - Diagnosis and Screening

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### SERUM LEVELS OF CHEMOKINES AND ADIPOKINES FOR NON-INVASIVE DETECTION OF ENDOMETRIOSIS IN A COHORT OF SYMPTOMATIC WOMEN

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**Objectives:** Because endometriosis induces a chronic inflammatory response, some chemokines and adipokines may be altered in the peripheral blood and become candidate diagnostic markers. We evaluated the diagnostic value of chemokines (eotaxin/CCL11, IP-10/CXCL10, MCP-1/CCL2) and adipokines (resistin and adiponectin) to detect endometriosis in women undergoing laparoscopy for gynecological conditions.

**Design:** We performed a prospective cohort study evaluating 77 women with chronic pelvic pain, infertility or ovarian cyst scheduled for laparoscopy.

**Materials and Methods:** Blood samples were collected from a peripheral vein and assayed for chemokines by CBA - Cytometric Bead Array Flex Set System (BD Biosciences, Heidelberg, Germany) according to the manufacturer's instructions. Adipokines were assayed using ELISA. Endometriosis was confirmed by histopathological examination of surgical specimens.

**Results:** Overall, the preoperative serum levels of all markers evaluated were similar in women with and without endometriosis. In a subset of patients with ultrasound image suggesting ovarian endometrioma (n=16), the subjects with this diagnosis eventually confirmed by laparoscopy and biopsy had lower serum IP-10 concentrations compared to those in whom an endometrioma was not found (114 +/- 33 pg/mL vs. 235 +/- 50 pg/mL, p=0.026).

**Conclusion:** Peripheral serum levels of eotaxin/CCL11, MCP-1/CCL2, resistin and adiponectin do not change significantly in endometriosis. Patients with endometrioma may have decreased IP-10 concentration. IP-10 is involved in the Th1-type immune response and has antiangiogenic properties. The pathophysiological implications of its reduction in women with endometrioma remains to be elucidated.

**Keywords:** Endometriosis, chemokines, adipokines

## Poster - Diagnosis and Screening

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### INCREASING THE EFFECTIVENESS OF ULTRASOUND IN OVARIAN ENDOMETRIOSIS

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**Objectives:** Transvaginal ultrasound (TVUS) is often the first examination ordered after clinical suspicion of endometriosis and plays an important role in its correct diagnosis. We propose to describe TVUS examination technique and imaging findings of ovarian endometriosis based on series of 50 patients with laparoscopic and histopathologic proved diagnosis.

**Design:** Cross-sectional study between February 2009 and March 2011 with 77 ovarian endometriomas in 50 premenopausal women. All patients were submitted to TVUS with systematically mapping of the entire pelvis. Diagnostic confirmation laparoscopic and histological in all cases.

**Materials and Methods:** Between February 2009 and March 2011, 50 patients with TVUS findings compatible with ovarian endometriosis were submitted to laparoscopic surgery and histopathological analyses. TVUS examinations performed by a single examiner, using ultrasound 22 IU (Philips, The Netherlands) and Aplio XG (Toshiba, Japan) and specific protocol for research endometriosis.

**Results:** The most frequent imaging finding was ovarian endometriomas (85%) with sizes ranging from 10 to 92 mm (mean size 26 mm). Histologic examination demonstrated 71 ovaries with endometriosis (92.2%) and only 06 ovaries without endometriosis (7.8%). Overall accuracy of TVUS was 88.3% (CI 95%: 81.1%-95.5%), with sensitivity of 90.1% (CI 95%: 83.2%-97.1%) and specificity of 66.7% (CI 95%: 28.9%-100.0%). Indirect sonographic features were observed in 74.6% of the sampling: ovarian adhesions in 46 patients (59,7%)—sensitivity 49.21% (CI 95%: 36.86%-61.55%) and specificity 90% (CI 95%: 71.41%-100%); periaxonal accumulation of viscous fluid in 23 patients (29,8%)—sensitivity 30.16% (CI 95%: 18.83%-41.49%) and specificity 100%; and hyperechoic foci of cyst walls in 23 patients (29,8%)—sensitivity 12.70% (CI 95%: 4.48%-20.92%) and specificity 90.0% (CI 95%: 71.41%-100%).

**Conclusion:** Beyond the classic endometriotic cysts other imaging findings can suggest the diagnosis of ovarian endometriosis. In this study TVUS proved effective in detecting early ovarian endometriosis, especially when supported by indirect features, such as ovarian adhesions, periaxonal viscous fluid collection, and hyperechoic foci of cyst walls.

**Keywords:** Endometriosis, ultrasound, diagnosis

## Poster - Diagnosis and Screening

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### COMPARISON OF HYSTEOSALPINGOGRAPHY AND VIDEOLAPAROSCOPY IN THE EVALUATION OF TUBAL IN INFERTILE PATIENTS WITH PELVIC ENDOMETRIOSIS.

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**Objectives:** To verify the agreement between videolaparoscopy and hysterosalpingography in the evaluation of tubal factor of infertile patients with endometriosis

**Design:** This is a cohort prospective study.

**Materials and Methods:** The study enrolled 237 female infertile women at outpatient clinic of the Tropical Institute of Reproduction Medicine and Menopause, Cuiabá, MT, Brazil. The patients evaluation included screening for infection diseases, transvaginal ultrasound, hysterosalpingography and videolaparoscopy. Agreement between methods was verified using Cohen's Kappa coefficient.

**Results:** At videolaparoscopy examination endometriosis was found in 181 (76.4%) patients. The prevalence of normal tubes using hysterosalpingography was (140/199) 70.3% and using videolaparoscopy was 81/170 (47.6%) Both methods, hysterosalpingography and videolaparoscopy, were performed in 169 patients with diagnostic of pelvic endometriosis. Concerning fallopian tube conditions, agreement was observed in 110 – patients (65.0% of the observations) and the number of agreements expected by chance would be 84.6 (50.0% of the observations). Kappa index was 0.301, 95% confidence interval of 0.16.1 to 0.440.

**Conclusion:** The strength of agreement between hysterosalpingography and videolaparoscopy to evaluate tubal factor in infertile women with pelvic endometriosis is poor

**Keywords:** Infertility, endometriosis, diagnosis

## Poster - Diagnosis and Screening

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### HOW RELIABLE IS OFFICE GEL SONOVAGINOGRAPHY (SVG) IN PREDICTING DEPTH OF INFILTRATION OF BOWEL DEEP INFILTRATING ENDOMETRIOSIS (DIE)?

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**Objectives:** To determine the accuracy of office gel sonovaginography in predicting the depth of infiltration of bowel DIE.

**Design:** A prospective observational study evaluating 20 patients with segmental resections for symptomatic bowel DIE.

**Materials and Methods:** Depth of infiltration of bowel DIE was recorded as involving the muscularis propria alone or with submucosal/mucosal layer at time of SVG. Depth of bowel infiltration was determined from the histopathology reports of each resected bowel specimen and compared with SVG prediction of depth of infiltration of bowel DIE.

**Results:** Segmental bowel resection for bowel DIE occurred in 10% of our series. Data was complete for 18/20. The PPV of SVG for the prediction of presence of DIE affecting the muscularis propria is 100%. The sensitivity, specificity, PPV, NPV, and test accuracy for submucosal/mucosal layer involvement were 71.4%, 64%, 55.5%, 78% and 67% respectively.

**Conclusion:** In our unit, SVG is a valuable tool in the recognition of bowel endometriosis. Whereas it can accurately predict infiltration of the bowel muscularis propria by endometriosis, it is less valuable in predicting submucosal/mucosa involvement.

**Keywords:** Svg, bowel die

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### URINARY SYMPTOMS AND URODYNAMIC FINDINGS IN WOMEN WITH PARAMETRIAL ENDOMETRIOSIS: AN EXPLORATORY STUDY.

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**Objectives:** Sometimes, deep infiltrating endometriosis (DIE) needs ample surgical resections, which can be followed by urinary problems. Considering the complex distribution of pelvic nerves and their symmetric relationship with the parametrium, we pre-operatively assessed the association between DIE in parametrium not only with specific urinary symptoms but also with urodynamic findings.

**Design:** Cross-sectional (pre-planned) observational study (Canadian Task Force Classification II-2) including a total of 50 women (ages 15-52 years) who were evaluated before undergoing laparoscopy for DIE during pre-operative diagnostic routine from June/2011 to August/2013 in Rio de Janeiro, Brazil.

**Materials and Methods:** Assessed urinary symptoms: urgency, perception of bladder fullness, incontinence, diurnal micturition, nocturia, dysuria/strangury, interrupted urine flow, Valsalva maneuver and feeling of incomplete urination. Urodynamic variables: maximum flow, post-voiding residue, sensitivity, complacency, maximum cystometric capacity (MCC), opening pressure, maximum pressure in urination, detrusor contractility (Schäffer's nomogram) and obstruction (Abrams-Griffiths's nomogram).

**Results:** Pre-operative diagnosis of DIE in parametrium (>5mm) was made by an experienced radiologist with basis on nuclear magnetic resonance imaging. The prevalence (95% confidence interval) of lesion in parametrium was 24.0% (95%CI:12.0-36.0%), including six severe cases in which DIE also infiltrated ureter and uterine artery. There was no woman with bilateral infiltrated parametrium. The prevalence of urinary symptoms was 32.0% (95%CI:20.0-46.0%) and they were significantly associated with DIE-lesion in parametrium (OR=4.2; 95%CI:1.1-16.2; p=.04). Concerning the association between specific symptoms and DIE in parametrium, the only significant symptom was interrupting voiding (OR=27.9; 95%CI:2.8-275.8; p<.01), though some tendencies (p>.05) were noticed. Associations were assessed through non-parametric Fisher's Exact test (2-sided).

**Conclusion:** Considering this sample of women in whom several sites were affected by DIE, the probability of pre-operative urinary symptoms or urodynamic findings being linked to DIE in parametrium couldn't be excluded. More, bilateral DIE in parametrium seems to be uncommon; it couldn't be evaluated because there were no cases.

**Keywords:** Urodynamic, parametrium, voiding.

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### THE INCIDENCE AND DIAGNOSTIC PROCESS UNTIL SURGICAL CONFIRMATION OF ENDOMETRIOSIS IN NORTHERN ISRAELI WOMEN –AN INSIGHT INTO THE DIAGNOSTIC DELAY AND POTENTIAL CAUSES

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**Objectives:** The goal of this study was to assess in women with surgically confirmed diagnosis of endometriosis the diagnosis process, diagnostic delay, clinical characteristics and the incidence of endometriosis in Haifa sub-district, Israel.

**Design:** A two stage cross-sectional study in Haifa sub-district , based on retrieval from 3 hospitals databases of women with surgically proven diagnosis of endometriosis between the years 2009-2011 was carried in order to calculate the incidence rates and thereafter telephone surveys was conducted.

**Materials and Methods:** After receiving approvals from the ethics committees approval from the three hospitals where most endometriosis cases are being diagnosed (Carmel, Rambam and Assuta), 135 women were interviewed regarding their diagnostic process prior to surgery as well as about demographics, symptoms onset, relevant medical history and medical appointments.

**Results:** The annual incidence rates of endometriosis increased from 29.8/100,000 (2009) to 41/100,000 (2011). The average age of symptoms onset was 17 (SD=8, median=14). The average time from symptoms onset to diagnosis was 18 years (SD=10, median=16). Fifty percent reported experiencing more than 7 symptoms before their first diagnosis. Women reported visiting an average of 4.1 physicians before diagnosis;93.3% of visits were to gynecologists. Only 16% were told during their first visit that their symptoms were suggestive of endometriosis. The diagnostic delay was longer: for women with earlier symptoms onset ( $r=-0.615$ ,  $P<0.001$ ), for Arab versus Jews (difference of 7.3 years,  $P<0.003$ ), for women with education level of  $\leq 12$  years (difference of 10 years,  $P<0.005$ ) and women with lower socioeconomic status ( $r=-0.19$ ,  $P<0.003$ ).

**Conclusion:** Increasing Annual incidence rates of endometriosis in Northern Israel and major diagnostic delay, urge the need to raise the awareness within women and physicians in Israel, especially within teenagers, Arabs and uneducated women, in order to decrease the diagnostic delay and potential social and economic burden of the disease.

**Keywords:** Diagnosis Incidence Endometriosis

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### PROFILING THE URINARY PROTEOME OF WOMEN WITH ENDOMETRIOSIS

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**Objectives:** The overall objective of this study is to identify non-invasive biomarkers able to screen for endometriosis at different stages. To establish whether there is a best selective time for biomarker detection by comparing early morning urine to urine collected during laparoscopic surgery to analyse the urinary proteome.

**Design:** This is a prospective cohort study at a tertiary referral hospital. Urine samples were collected from three women undergoing laparoscopic surgery. Each woman provided a first morning urine sample prior to arrival at hospital and a second sample during her laparoscopic procedure when the patient was catheterised.

**Materials and Methods:** Urinary proteins were extracted and concentrated using 10kDa Amicon Ultra Filter (Millipore) and separated using 2D gel electrophoresis. Progenesis SameSpot software (Nonlinear Dynamics) was used to analyse gel images. Proteins of interest were subjected to trypsin digestion and identified by MALDI-TOF mass spectrometry (MS) and MASCOT searching (Matrix Science).

**Results:** Proteins common to and in high or low abundance between the first morning and surgical urine samples were detected and selected for MS identification and are currently undergoing analysis. A small number of spots are promising. Further analyses may lead us to nominate possible biomarkers that could be specific for assessment of endometriosis and possible development of a diagnostic ELISA assay. Initial study has identified around 140 discrete spots in the early morning urines and only around 40 in those collected in theatre.

**Conclusion:** The urinary proteome of a first pass morning sample is different when compared to the urine collected during surgery. The early morning specimen offers many more spots and appears preferable for further detailed study.

**Keywords:** Endometriosis, proteomics, biomarkers

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### ULTRASOUND DIAGNOSIS OF DEEP ENDOMETRIOSIS INVOLVING BLADDER, VAGINAL FORNIX AND SIGMOID: A CASE REPORT

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**Objectives:** To describe a case report of deep endometriosis in bowel, bladder and vaginal fornix diagnosed by ultrasound with bowel preparation.

**Design:** A case report of deep endometriosis with ultrasound diagnosis

**Materials and Methods:** A case report of a 36-year-old woman, admitted to our service with recurrence lower abdominal pain and intense painful urination during the menstrual period. transvaginal and abdominal ultrasound with bowel preparation revealed deep endometriosis.

**Results:** A 36-year-old woman, with recurrence lower abdominal pain and intense painful urination, during the menstrual period. Transvaginal and abdominal ultrasound with bowel prepared revealed: 1-large bladder wall tumor infiltrated occupying the basis of bladder tangent left meatus; 2- an extensive injury in posterior vaginal fornix infiltrating both muscular and mucosis layers, 3-an extended infiltration of sigmoid muscular layer kinking the bowel segment handle 4- left ovarian endometrioma with 200ml. Colonoscopy and magnetic resonance confirmed the ultrasound finds. Consequently, a deep endometriosis was suspected before surgery. a laparoscopic surgery was performed with vesical lesion resection without affecting left meatus, excision of the vaginal fornix injury and sigmoidectomy and anastomosis. Histopathological examination was consistent with deep endometriosis. The postoperative course was uneventful.

**Conclusion:** Transvaginal ultrasonography with bowel preparation is an important technique to a more appropriate surgical strategy to be implemented in cases of deep endometriosis.

**Keywords:** Deep endometriosis, ultrasound, laparoscopy

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### AN ELISA TEST DEVELOPMENT AND CLINICAL VALIDATION FOR A NEW SERUM MARKER OF ENDOMETRIOSIS

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**Objectives:** Symptoms in women with mild endometriosis are not easily recognized in primary care or even by women themselves. This study aims to identify sensitive and specific serum markers and develop a low invasive method for screening women with endometriosis at early stage before further invasive diagnosis and the treatment.

**Design:** Serum samples collected from women with and without endometriosis

**Materials and Methods:** Serum proteomics and enzyme-linked immunosorbent assay

**Results:** By proteomic approaches, a serum protein, alpha 1 antitrypsin (A1AT) was identified to be significantly increased in patients with endometriosis at early stage. Additionally, the level of A1AT was decreased in patients receiving gonadotropin-releasing hormone analog (GnRHa) treatment. Monoclonal antibodies specifically recognized A1AT were produced. Their sensitivity and specificity were higher compared to the commercially available antibodies for detecting the expression of A1AT in women with mild and moderate endometriosis. An enzyme-linked immunosorbent assay (ELISA) test was designed and developed for screening high risk patients with endometriosis. A 2-year randomized and double-blind clinical trial in Taipei Medical University Hospital is ongoing for evaluating the newly developed diagnostic method for endometriosis.

**Conclusion:** Alpha 1 antitrypsin can be a potential serum marker for screening of patients with endometriosis at early stage..

**Keywords:** Diagnosis, Endometriosis

Poster - Endometrioma and ovarian reserve

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**THE DECLINE OF SERUM ANTI-MÜLLERIAN HORMONE LEVEL FOLLOWING LAPAROSCOPIC OVARIAN CYSTECTOMY IN ENDOMETRIOMA AND OTHER BENIGN CYSTS: A PROSPECTIVE COHORT STUDY**

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**Objectives:** To identify the most important factor in predicting ovarian reserve following laparoscopic ovarian cystectomy and to evaluate whether there is any difference in the postoperative decline of ovarian reserve between women with endometrioma and those with other benign ovarian cysts.

**Design:** A prospective cohort study in a university hospital

**Materials and Methods:** We recruited a total of 102 patients who had undergone laparoscopic ovarian cystectomy due to endometrioma (n=68) or other benign ovarian cyst (n=34). The serum AMH levels were measured preoperatively and 3 months following operation, and the rate of decline following ovarian cystectomy were analyzed with several parameters.

**Results:** The serum AMH level was obviously decreased at 3 months following operation ( $5.07 \pm 3.00$  vs.  $3.39 \pm 2.13$  ng/mL, mean  $\pm$  SD,  $P < 0.001$ ). Adjusting several parameters, we could see that the bilaterality of the ovarian cyst is the only significant factor ( $P < 0.001$ ) in predicting the rate of AMH decline following operation. The rate of AMH decline was not different between endometrioma group and other benign ovary cyst group.

**Conclusion:** The bilaterality is the only significant factor in predicting the rate of decline of AMH level following laparoscopic ovarian cystectomy. The rate of decline of AMH level following operation seems to be comparable between endometrioma group and other benign ovary cyst group.

**Keywords:** AMH;endometrioma;cystectomy

Poster - Endometrioma and ovarian reserve

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**COMPARISON OF IMPACT OF LAPAROSCOPIC CYSTECTOMY ON OVARIAN RESERVE BETWEEN PATIENTS WITH ENDOMETRIOMA AND THOSE WITH OTHER BENIGN OVARIAN CYST**

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**Objectives:** The aim of this study was to evaluate the difference of the change of ovarian reserve immediately after laparoscopic unilateral ovarian cystectomy between patients with endometrioma and those with other benign ovarian cyst.

**Design:** This study suggests that immediate postoperative decline of AMH levels after unilateral ovarian cystectomy may be higher in patients with endometriosis than those with other benign ovarian cysts except mature teratoma.

**Materials and Methods:** Fifty-nine patients who were undergoing laparoscopic unilateral ovarian cystectomy for endometrioma (n=24) and other benign ovarian cyst (n=35) participated. Preoperative and postoperative day 3 serum samples were collected and assayed for AMH levels, and changes between the two samples were analyzed.

**Results:** Preoperative AMH levels were not significantly different between patients with endometrioma ( $5.07 \pm 2.72$  ng/ml) and those with other benign cyst ( $6.26 \pm 3.29$  ng/ml). Postoperative day 3 AMH levels were  $3.69 \pm 1.87$  ng/ml in patients with endometrioma and  $4.91 \pm 2.57$  ng/ml in the others, both were significantly decreased compared with preoperative levels. There was no significant difference in the rate of decline between patients with endometrioma and those with other benign cyst ( $26.20 \pm 20.97$  vs.  $20.43 \pm 20.22\%$ ,  $P = 0.343$ ), but the rate of decline was significantly higher in endometrioma group than other benign cyst group after excluding mature teratoma ( $26.20 \pm 20.97$  vs.  $12.03 \pm 18.56\%$ ,  $P = 0.046$ ).

**Conclusion:** No statistically significant difference was found in the rate of decline between endometrioma group and mature teratoma group.

**Keywords:** Endometrioma anti-Müllerian hormone

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**MORPHOLOGIC CHARACTERISTICS OF OVARIAN TISSUE ADJACENT TO THE CYST WALL OF ENDOMETRIOMA**

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**Objectives:** Some studies reported that ovarian reserve declines after laparoscopic cystectomy of endometriomas. The aim of this study was to evaluate the thickness of the ovarian parenchyma inadvertently excised along with the cyst wall and follicle loss in ovarian tissue after laparoscopic excision of endometriomas.

**Design:** This prospective study was conducted in RSMU City Clinical Hospital №31 during the last year. Our study included 32 reproductive aged women, who underwent laparoscopic cystectomy for endometriomas.

**Materials and Methods:** We evaluated the thickness of the cyst wall, removed ovarian tissue. After we calculated the number of follicles in each specimens. The samples including ovarian tissue were morphologically graded on a semi-quantitative scale from 0 to 4.

**Results:** The presence of ovarian cortex adjacent to the cyst wall was detected in all patients. There were statistical inverse relationship between the thickness of ovarian parenchyma removed and the thickness of the cyst wall. The ovarian tissue removed closed to the ovarian hilus was significantly higher,  $p < 0,0001$ , which contained follicles grade 2 significantly higher,  $p = 0,05$ . There was statistically significant inverse relationship between patient age and number of follicles. Most of removed follicles were primordial follicles (75%), which mainly determine ovarian reserve.

**Conclusion:** This study suggest that laparoscopic cystectomy of endometriomas is associated with a removal of ovarian tissue and follicular loss. Newer surgical techniques that cause less harm to the ovarian tissue may be developed in the future.

**Keywords:** Endometrioma, ovarian reserve.

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**THE LAPAROSCOPIC SUCTION OF THICK FLUID CONTENT IN LARGE ENDOMETRIOMA BY USING SPECIAL MULTIPLE-HOLE SUCTION-CATHETER**

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**Objectives:** In the laparoscopic suction of fluid, sometimes content in large endometrioma is very thick and it doesn't aspirated by usual suction-catheter easily. Furthermore abdominal spillage is somewhat dangerous due to malignant potential. The special suction-catheter is needed for suction of thick content without obstruction

**Design:** We investigated usefulness of special multiple-hole suction-catheter for laparoscopic suction of thick content in endometrioma. The study was performed university hospital. The statistical analysis was done by SPSS 13.0.

**Materials and Methods:** We did the 31 laparoscopic operations for large endometrioma with thick content by special multiple-hole suction-catheter (Group A). They were compared with 36 patients who received operation without this suction-catheter (Group B). The duration of suction of content, amount of abdominal spillage of content were compared.

**Results:** The age-distributions and tumor sizes between Group A ( $31.0 \pm 3.6$ ,  $6.4 \pm 1.2$  cm) and B ( $30.8 \pm 6.8$ ,  $5.9 \pm 0.7$  cm) were not significantly different. The durations of suction of thick fluid contents were very shorter ( $P < 0.01$ ) in Group A ( $1.2 \pm 1.3$  min.) than Group B ( $7.3 \pm 3.4$  min.). The amount of abdominal spillage were much lesser ( $P < 0.01$ ) in Group A ( $0.1 \pm 0.2$  ml) than Group B ( $5.2 \pm 3.1$  ml).

**Conclusion:** Therefore if large endometrioma has very thick fluid content, the laparoscopic suction of thick fluid content can be done easily with minimal abdominal spillage by using special multiple-hole suction-catheter, and it can be helpful for duration of operation and prevention of malignant spillage to abdominal cavity.

**Keywords:** Suction-catheter spillage endometrioma

Poster - Endometrioma and ovarian reserve

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THE POSTOPERATIVE DECLINE IN SERUM AMH LEVELS IN PATIENTS WITH ENDOMETRIOSIS

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**Objectives:** To compare the pre- and post-operative serial changes of serum anti-Müllerian hormone (AMH) levels for evaluating the impact of ovarian cystectomy in patients with endometriosis.

**Design:** Prospective clinical study. A total of seventy five patients who were undergone ovarian cyst enucleation were prospectively included from April 2011 to May 2012 in a single center.

**Materials and Methods:** The 59 patients had endometrioma (group A) and 16 patients (group B) had benign ovarian cysts as control. We had taken AMH levels at operation and in 1-2 months after operation. Exclusion criteria was age  $\geq$  40yrs, irregular menstruation, previous ovarian surgery, and PCOS.

**Results:** The mean age and BMI was not significantly different in group A and B ( $30.5 \pm 4.3$  vs.  $28.5 \pm 5.7$ , yrs;  $20.0 \pm 4.4$  vs.  $19.8 \pm 5.4$ , kg/m<sup>2</sup>). The mean cyst size was larger in group B ( $7.4 \pm 3.1$  vs.  $4.9 \pm 1.8$ , cm,  $p=0.0001$ ). Post-operative AMH levels was significantly lower in group A than in group B ( $2.8 \pm 1.8$  vs.  $4.9 \pm 4.0$ , ng/ml,  $p=0.004$ ). In group A, pre- and postoperative AMH levels significantly was decreased ( $p=0.0001$ ). The rate of decline between pre- and post-operative AMH (ng/ml) was 21.4% and 17.8% in group A and B. In group A, there was correlation in the rate of AMH decline with BMI ( $r=-0.332$ ,  $p=0.01$ ) and preoperative AMH levels ( $r=0.451$ ,  $p=0.0001$ ).

**Conclusion:** The post-operative serum AMH levels in the patients with endometrioma could be worse than other cyst. It should be considered in the case of surgery.

**Keywords:** ovarian reserve, AMH

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**TRANSVAGINAL ULTRASOUND AFTER BOWEL PREPARATION FOR THE PRE-AND-POST OPERATIVE EVALUATION OF OVARIAN RESERVE BY ANTRAL FOLLICLE COUNT AND ANTI-MULLERIAN HORMONE IN INFERTILE WOMEN WITH ENDOMETRIOMAS**

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**Objectives:** To noninvasively evaluate ovarian reserve by the assessment of antral follicle count and serum anti-Müllerian hormone, as well as the extensiveness of the deep infiltrative endometriosis (DIE) in the pre-and in the immediate postoperative interval following laparoscopic surgery for removal of DIE associated or not with endometriomas in infertile women

**Design:** Prospective observational study for the evaluation of infertile women undergoing extensive laparoscopic surgery for deep infiltrating endometriosis. The postoperative interval for evaluation was from 3 to 6 months.

**Materials and Methods:** Ovarian reserve was assessed by antral follicle count and anti-Müllerian hormone (AMH) levels. All women were screened for DIE and OMAS by transvaginal ultrasound after bowel preparation (TVSBP). AFC was evaluated by the total number of 2-10 mm follicles. Paired Wilcoxon test was used; significance  $p < 0.05$ .

**Results:** 345(23.3%) women fulfilled surgical requirements. 106 women (30.7%) underwent laparoscopy (LSC) and 96 (90.5%) underwent a post-op TVSBP 3-6 months interval after the original surgery. The number of OMAS per patient was  $1.7 \pm 1.1$  for the right ovary (ROv) and  $1.4 \pm 0.6$  for the left ovary (LOv). From 41 OMAS, 33 (80.5%) were fully resected. Thick adhesions limited preoperative ROv and LOv mobility in 48% and 61%. After resection of the adhesions, mobility restriction was reduced to 17% ( $p < 0.001$ ) and 23% ( $p < 0.001$ ), respectfully. Preoperative AFC in the ROv and LOv were  $7.6 \pm 4.0$  and  $6.8 \pm 4.2$  and were maintained in the postoperative for the ROv as  $7.5 \pm 4.5$ ;  $p = 0.985$  and for the LOv as  $6.9 \pm 4.3$ ;  $p = 0.871$ . Pre and postoperative AMH levels did not varied significantly as  $1.58 \pm 2.39$  and  $1.74 \pm 1.26$  ng/mL.

**Conclusion:** The use of pre-and-postoperative TVSBP, AFC and serum AMH levels after LSC for resection of DIE and OMAS demonstrated to be an excellent noninvasive tool for the evaluation of extensive LSC and to postoperatively prospect ovarian wellbeing and reproductive future.

**Keywords:** DIE, ovarian reserve

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**TWO PORT ACCESS VERSUS FOUR PORT ACCESS LAPAROSCOPIC OVARIAN CYSTECTOMY**

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**Objectives:** This study was conducted to compare the surgical outcomes between two-port access and four port access laparoscopic ovarian cystectomy.

**Design:** Comparing laparoscopic two port and four port methods for ovarian cystectomy

**Materials and Methods:** Four hundred and eighty nine patients who had received two port access laparoscopic ovarian cystectomy (n=175) and four port access laparoscopic ovarian cystectomy (n=314) were analyzed retrospectively. The data were compared between the bilaterality of the cysts and cystic diameter of less than 6 cm and 6 cm or more.

**Results:** There were no significant differences in patient's age, parity, body weight, body mass index and history of previous surgery between the two-port and four-port access laparoscopy group. Bilaterality of ovarian cysts was more in four port access laparoscopy group (13.7% vs 32.5%, P=0.000). There were no significant differences in operation time, hemoglobin change, hospital stay, adhesiolysis, transfusion, and insertion of hemo-vac between the two-port and four-port access laparoscopy group for size matched compare. However additional analgesics were more in four-port access laparoscopy group for unilateral ovarian cystectomy.

**Conclusion:** Two-port access laparoscopic surgery was feasible and safe for unilateral and bilateral ovarian cystectomy compare with four port access laparoscopic surgery.

**Keywords:** Ovarian cystectomy, Laparoscopy

Poster - Endometrioma and ovarian reserve

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**MAINTAINING MORPHOLOGICAL CHARACTERISTICS OF THE ENDOMETRIOTIC CYSTECTOMY TISSUE BY GOOD TECHNIQUE FOR GOOD OVARIAN RESERVE**

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**Objectives:** To assess the value of a semiquantitative scale grading by histology of the endometriotic cystectomy tissue in comparison to ovarian reserve with peeling technique of cyst

**Design:** A prospective observational study in a tertiary care hospital over two years in 2010-2012 was done in patients with ovarian endometriomas undergoing surgical removal by careful dissection and decrease cautery use. All the tissues were analyzed with morphological characteristics by grading and compared with ovarian reserve tests.

**Materials and Methods:** Ovarian volumes, antral follicle counts, stromal blood flows were assessed before and after cystectomy, same was correlated with the histological grading of 0,1,2,3,4 by the absence or presence of primordial, primary, secondary follicles. Grades 0-4 were grouped as I (no loss of follicles) & 3-4 as II (loss of follicles)

**Results:** Analysis of 88 cystectomy tissues showed that there was no loss of follicles in 72.7% and loss in 27.2% in Group I & II respectively. Mean stromal peak systolic velocity (PSV) of the operated ovary were  $6.8 \pm 4.57$  before and  $7.1 \pm 3.55$  after surgery, p value of  $P=0.48$ . The mean Day 2 FSH mean antral follicles preoperatively and postoperatively were statistically not significant. Cysts with preoperative diameter less than or equal to 5 cms showed greater loss of follicles compared with cysts with preoperative diameter greater than or equal to 5.1 cms, which was statistically significant. According to ASRM staging, In group I and II it was 78.9% and 21.1% belonging to Mild and Moderate to severe endometriosis respectively.

**Conclusion:** There was no statistically significant difference between the ovarian reserve parameters which might be explained as a result of the gentle surgical technique, as we preferred meticulous hemostasis instead of using excessive bipolar forceps electro coagulation especially in hilar areas.

**Keywords:** Cystectomy, ovarian reserve

## Poster - Endometrioma and ovarian reserve

P-52

### LONGITUDINAL FOLLOW UP OF POST-OPERATIVE OVARIAN RESERVE IN INFERTILE WOMEN HAD LAPAROSCOPIC CYSTECTOMY FOR ENDOMETRIOMA AFTER DRAINAGE AND ORAL DIENOGEST THERAPY

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**Objectives:** Cystectomy is the choice of therapeutic option for ovarian endometrioma. Three step management utilizing GnRH agonist and cyst wall vaporization had been shown to be beneficial. In this study, we tried to evaluate the efficacy of medico-surgical approach with dienogest, a synthetic progestin, in infertile women had cystectomy for endometriomas.

**Design:** First- and second-look laparoscopy were performed at an interval of 3 months and dienogest (2mg) was administered between these two intervention. Serum AMH levels were prospectively measured before and after surgery.

**Materials and Methods:** Six infertile women under 37 years were enrolled. First-look laparoscopy (FLL) was performed to irrigate the cyst. Then, oral dienogest were given daily for 3month. Second-look laparoscopy (SLL) was carried out to perform cystectomy (hemilateral cystectomy or cyst wall coagulation for bilateral case). Serum AMH levels were determined by ELISA.

**Results:** Size of endometrioma was significantly decreased at SLL compared to that of FLL ( $4.7\pm 1.4$  vs.  $2.3\pm 0.8$ cm,  $P=0.0008$ ). We did not find any significant change in r-ASRM score between two surgeries. Serum AMH levels decreased by  $21\pm 22\%$  at FLL and by  $39\pm 22\%$  across SLL. One month after SLL, serum AMH level further decreased by  $63\pm 13\%$  comparing to basal (pre-FLL) AMH values. Multivariate ANOVA revealed that severity of adhesion at FLL significantly contributed to these changes. Three women showed partial recovery of serum AMH levels at 6 month after SLL. Two women conceived within one year after SLL.

**Conclusion:** Serum AMH levels may be modulated by types of surgical manipulations and perioperative medical treatment. Protective effects of irrigations and progestin therapy against cystectomy are limited. Severity of pelvic adhesion may be associated with post-surgical decline in ovarina function. Further studies are needed to strengthen our current findings.

**Keywords:** endometrioma, cystectomy, AMH

Poster - Endometrioma and ovarian reserve

P-53

THE INCIDENCE OF LEFT SIDED OVARIAN ENDOMETRIOMA

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**Objectives:** The aim of this study is determine the incidence of Left sided ovarian endometrioma.

**Design:** Case histories of 35 patients with endometrioma were analyzed, from March 2010 to June 2011.

**Materials and Methods:** The characteristics of patients and the incidence of laterality were determined by analysis using chi-square and t-test

**Results:** the data revealed that 30 cases diagnosed by endometrioma after surgery were located on the left side mass (76%),12 cases were located on the right (30%) and 11 cases were bilateral (8.3%). In endometrioma patients, cases with left sided pelvic painful mass is more frequent than right side painful mass.

**Conclusion:** This study determine the percentage of left-sided ovarian endometrioma.

**Keywords:** Left sided endometrioma

## Poster - Endometriosis and cancer

P-54

### LIFETIME RISK OF OVARIAN CANCER BASED ON ENDOMETRIOSIS AND OTHER RISK FACTORS

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**Objectives:** Ovarian cancer is rare but deadly. Protective factors include oral contraceptives (OCs), tubal ligation, and parity. Risk factors include endometriosis, family history of ovarian cancer, and common susceptibility alleles. We identified combinations of these risk/protective factors that put women at low and high risk for ovarian cancer.

**Design:** Pooled analysis of case-control studies from the Ovarian Cancer Association Consortium.

**Materials and Methods:** Applying published risk estimates for risk/protective factors to multiplicative models, the relative risks and variances for every combination were calculated. To convert to absolute risks we divided each combination-specific relative risk by the frequency-weighted average of all the combination-specific relative risks and scaled to a weighted average of unity.

**Results:** 214 combinations of risk/protective factors were observed among 4497 cases and 4497 controls. As compared to a U.S. registry average lifetime risk of 1.37%, lifetime risks here ranged from 0.35% to 8.78%. Women in the lowest five categories (<0.5% lifetime risk) all used OCs 5+ years, bore children, and had no family history and no endometriosis. Women with the highest lifetime risk (> 5%) all had either a family history or endometriosis; no tubal ligation; never used OCs (7/8 categories). Genetic risk profiles were diverse. Comparing lifetime risks showed, for example, a woman at moderate risk (4.3%) because of no tubal ligation and nulliparity (but no family history and no endometriosis) would reduce her risk to 1.7% if she used OCs for 5+ years.

**Conclusion:** A >20-fold differential in risk resulted from various risk/protective combinations. More specifics will be shown for the impact of oral contraceptive use and tubal ligation as prevention modalities for ovarian cancer specifically among women with endometriosis.

**Keywords:** Ovarian cancer, epidemiology

Poster - Endometriosis and cancer

P-55

**PROGNOSTIC ANALYSIS OF ENDOMETRIOID EPITHELIAL OVARIAN CANCER WITH OR WITHOUT ENDOMETRIOSIS: A 12-YEAR COHORT STUDY OF CHINESE PATIENTS**

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**Objectives:** Clinicopathological characteristics and possible prognostic factors among women with endometrioid epithelial ovarian cancer (EEOC) with or without concurrent endometriosis were investigated to find the association between endometriosis and endometrioid epithelial ovarian cancer.

**Design:** Medical charts of patients with EEOC who were treated at Peking Union Medical College Hospital from 2002 through 2012 were searched. Clinicopathological characteristics (age, symptoms, Ca125 levels, tumor size, stage, et al.) were compared between the two groups and survival analysis was performed after a median follow-up time of 40.5 months.

**Materials and Methods:** Statistical association between the two groups and the clinicopathological variables were examined with chi-square test or Fisher exact tests as indicated. Survival comparisons were obtained using the logrank test in an unadjusted Kaplan-Meier model. Cox proportional hazards regression were used of multivariate analysis.

**Results:** Of 188 patients with EEOC, concurrent endometriosis was identified in 32 (17.0%). Patients with concurrent endometriosis were approximately 5 years younger, more likely to be premenopausal, more likely to have an early stage of EEOC, and less likely to have high-grade tumors compared to those without endometriosis. The univariate analysis showed that concurrent endometriosis was a significant prognostic factor for disease-free survival, but this association did not remain in the multivariate analysis.

**Conclusion:** Women with EEOC and concurrent endometriosis were younger, had earlier-stage disease and with a higher likelihood of low-grade tumors and had longer disease-free survival when compared to those without endometriosis. Endometriosis-associated ovarian cancer might be an entity distinct from typical EEOC.

**Keywords:** Endometriosis, ovarian carcinoma

Poster - Endometriosis and cancer

P-56

**GONADOTROPIN-RELEASING HORMONE AGONISTS FOR PREVENTION OF CHEMOTHERAPY-INDUCED OVARIAN DAMAGE IN PATIENTS WITH GYNECOLOGIC CANCER.**

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**Objectives:** To determine whether Gonadotropin-releasing hormone agonists (GnRHa) administration before and during chemotherapy for gynecologic cancer could preserve post-treatment ovarian function in young women.

**Design:** This study was a retrospective cohort study and medical record review was done.

**Materials and Methods:** Thirty-five patients with gynecologic cancer of who had gynecologic surgery with unilateral ovarian preservation were included in the study. Patients received combined GnRHa and chemotherapy. Return of spontaneous menstruation and ovulation was checked. Hormonal changes (FSH, LH, E2, P) during and after the completion of chemotherapy was evaluated.

**Results:** Twenty patients were ovarian germ cell tumor, eight patients were uterine cervical cancer, four patients were endometrial cancer, and three patients were epithelial ovarian cancer. Twelve patients with cervical cancer and endometrial cancer were performed hysterectomy. 20 out of 23 patients (87.0%) resumed menses and 14 patients (60.9%) resumed spontaneous ovulation within 2-9 months of termination of the GnRHa/chemotherapy co-treatment; three patient (13.0%) experienced hypergonadotrophic amenorrhoea and ovarian failure 7 months after treatment. All twelve patients who received hysterectomy showed normal ranged hormone level 8-12 months after completion of treatment.

**Conclusion:** GnRHa administration before and during combination chemotherapy for gynecologic cancer may preserve post-treatment ovarian function in young women. Long-term and large scale studies are necessary

**Keywords:** GnRHagonist, ovarian function

Poster - Endometriosis and cancer

P-57

**PROGNOSTIC ANALYSIS OF ENDOMETRIOID EPITHELIAL OVARIAN CANCER WITH OR WITHOUT ENDOMETRIOSIS: A 12-YEAR COHORT STUDY OF CHINESE PATIENTS**

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**Objectives:** Clinicopathological characteristics and possible prognostic factors among women with endometrioid epithelial ovarian cancer (EEOC) with or without concurrent endometriosis were investigated to find the association between endometriosis and endometrioid epithelial ovarian cancer.

**Design:** Medical charts of patients with EEOC who were treated at Peking Union Medical College Hospital from 2002 through 2012 were searched. Clinicopathological characteristics (age, symptoms, Ca125 levels, tumor size, stage, et al.) were compared between the two groups and survival analysis was performed after a median follow-up time of 40.5 months.

**Materials and Methods:** Statistical association between the two groups and the clinicopathological variables were examined with chi-square test or Fisher exact tests as indicated. Survival comparisons were obtained using the logrank test in an unadjusted Kaplan-Meier model. Cox proportional hazards regression were used of multivariate analysis.

**Results:** Of 188 patients with EEOC, concurrent endometriosis was identified in 32 (17.0%). Patients with concurrent endometriosis were approximately 5 years younger, more likely to be premenopausal, more likely to have an early stage of EEOC, and less likely to have high-grade tumors compared to those without endometriosis. The univariate analysis showed that concurrent endometriosis was a significant prognostic factor for disease-free survival, but this association did not remain in the multivariate analysis.

**Conclusion:** Women with EEOC and concurrent endometriosis were younger, had earlier-stage disease and with a higher likelihood of low-grade tumors and had longer disease-free survival when compared to those without endometriosis. Endometriosis-associated ovarian cancer might be an entity distinct from typical EEOC.

**Keywords:** Carcinoma, epidemiology, endometriosis

Poster - Endometriosis and cancer

P-58

**THE OCCURENCE OF ENDOMETRIOSIS WITH OVARIAN CARCINOMASIS NOT PURELY COINCIDENTAL**

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**Objectives:** To explore the association between epithelial ovarian cancer(EOC) and common benign gynecological disorders.

**Design:** The medical records of 226 patients with EOC treated at Peking Union Medical College Hospital between March 2012 were reviewed .Histological evaluations had been performed to determine the presence of coexisting pelvic endometriosis (n=17),uterine leiomyoma(n=66),adenomyosis(n=22),or endometrial polyps(n=17).

**Materials and Methods:** Statistical association between the two groups and the clinicaopathological variables were examined with chi-square test or Fisher exact tests as indicated.

**Results:** Coexistence of endometriosis occurred in 35.3% and 36.4%of cases of the clear cell and endometrioid subtypes of EOC histology respectively.Endometriosis was more likely associated with clear cell or endometrioid ovarian carcinoma, but less likely with high grade serous cancer.No defferences were observed in the concurrence of uterine myoma,adenomyosis or endometrial polyps among the different subtypes of EOC.

**Conclusion:** In contrast to other common benign gynecological disorders, endometriosis showed close relationships with endometrioid subtypes of EOC specifically

**Keywords:** Endometriosis, ovarian carcinomas

## Poster - Endometriosis and cancer

P-59

### CERVICAL CANCER AND DEEP ENDOMETRIOSIS: A CASE REPORT

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**Objectives:** Objective: To narrate a case of cervical cancer and deep endometriosis in young nulliparous woman

**Design:** Design: A case report with 10 months follow-up

**Materials and Methods:** Patient: female, 29 years, student, couple, menarche 14 years, first intercourse 16 years, nulliparous, irregular use of condom, cervical biopsy CIN III, dyspareunia and pelvic pain, in first consultation at Santa Casa de Porto Alegre Gynecologic Department, 2012 september.

**Results:** Description: Physical examination: exofitic tumor 3 cm diameter involving vaginal fornix, and nodule retrocervical hardened to touch. Cervical biopsy: epidermoid carcinoma, stage IIA1. Magnetic ressonance image: ovary and peritoneal endometriosis adjacent to left internal iliac artery, cervical lesion 3.2 cm without parametrial invasion, retrocervical nodule invading rectosigmoid muscular wall and posterior vaginal fornix (endometriotic origin or spread cervical cancer). CA-125: 49. Sigmoidoscopy: normal. As discussed with patient and in multidisciplinary staff, we decide by videolaparoscopy with oophoropexy, retrocervical lesion and lymphonode biopsies and hypogastric ligation if necessary. Pathology: endometriosis (retrocervical, peritoneal and lymphonodal capsule). The patient was submmited to chemotherapy plus radiotherapy and brachithery. Follow-up: amenorrhea and hormones compatibles with menopause since the end of radiation, using estrogen replacement therapy.

**Conclusion:** Conclusion: There are few reports that relate both conditions. The decision to indicate chemorradiation, in this case, was based at risk of radiotherapy after radical surgery and anastomotic leakage.

**Keywords:** Cancer, deep endometriosis

## Poster - Endometrium

P-60

### THE MENSTRUATING MOUSE MODEL FOR PRECLINICAL ENDOMETRIOSIS RESEARCH A FIRST STEP IN THE VALIDATION OF A NOVEL RODENT MODEL FOR ENDOMETRIOSIS

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**Objectives:** In order to standardize a menstruating mouse model, it is important to ensure premenstrual decidualization via the stimulus of intra-uterine oil injection in a predictable way. We hypothesize that intra-uterine oil injection via laparoscopy or laparotomy will result in a higher bicornuate decidualization (100%) than transvaginal intra-uterine oil injection (50%).

**Design:** 40 ovariectomized C57Bl/6J mice were subcutaneously injected with estradiol (100ng/day; 3 days), subcutaneously implanted with a progesterone pellet (serum levels: 22±8.1ng/ml), followed by estradiol injections (5ng/day; 3 days). Oil (20µl/horn) was injected in the uterus to induce decidualization, pellet removal was 49 hours later, followed by hysterectomy after 4-6 hours.

**Materials and Methods:** Endometrial decidualization was quantified macroscopically (uterine weight) and microscopically (assessment of endometrial surface area after exclusion of myometrium and lumen) after haematoxylin and eosin staining of uterine sections. ELISA tests were performed to measure serum estrogen and progesterone levels.

**Results:** The proportion of animals with bicornuate decidualization was higher during laparoscopic (5/6, 84%) and laparotomic (8/9, 89%) injection than during vaginal injection (3/10, 30%). Unicornuate decidualization was absent in both laparoscopic (0/6, 0%) and laparotomic (0/9, 0%) groups but was observed in the vaginal group (4/10, 40%). Relative uterine weight was higher in both the laparotomic (199.6±100.4mg, p<0.01) and the laparoscopic (209.2±145.5mg, p<0.05) groups compared to the sham group (70.39±98.33mg). The endometrial surface area was higher in the laparotomic (3.09±0.66 mm<sup>2</sup>, p<0.05) and laparoscopic (3.06±1.53 mm<sup>2</sup>, p<0.05) groups than in the sham group (0.67±1.16 mm<sup>2</sup>). Serum E2 as P4 concentrations were comparable (p>0.05) between animals with and without decidualized endometrium.

**Conclusion:** Although we did not obtain 100% bicornuate decidualization, the proportion of animals with bicornuate decidualization was higher in the laparoscopic (84%) and laparotomic (89%) groups than in the vaginal injection group (30%). Since laparotomy was associated with inflammation and adhesions, laparoscopy is the method of choice to induce endometrial decidualization.

**Keywords:** Decidualization, menstruation, mouse

## Poster - Endometrium

P-61

### NERVE FIBER DETECTION IN ENDOMETRIUM BIOPSIES FOR SEMI-INVASIVE DIAGNOSIS OF ENDOMETRIOSIS.

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<sup>1</sup> Private Uba, Buenos Aires, Argentina

**Objectives:** Show that the density of sensory nerve fibers of small diameter (type C) per mm<sup>2</sup> in the functional layer of the endometrium is higher among patients with endometriosis than among those without the disease.

**Design:** Prospective, double blind and a cross-sectional study

**Materials and Methods:** 42 patients with clinically suspected endometriosis which underwent diagnostic laparoscopy and endometrial biopsy (with endometriosis 24, without 18). The study included endometrial samples by immunohistochemical analysis with rabbit polyclonal antibody against the antigen PGP 9.5, mouse monoclonal anti CGRP polyclonal antibody sheep anti NPY and rabbit polyclonal antibody anti VIP.

**Results:** The average value of the density of nerve fibers stained with PGP 9.5 antibody in patients with endometriosis was 0.91 (+ / - 1.38) and the median of 0.32, without endometriosis averaged value 0.089 (+ / - 0.19). Statistical analysis was performed using the R Commander Version 1.8-3, on the 0.05 significance level. We used a nonparametric hypothesis test and found a significant difference between groups ( $p = 0.0005996$ ). The rest of the marks showed no conclusive data. Distribution was also assessed and measured mm<sup>2</sup> central variable to see if the surfaces of biopsies were comparable ( $p = 0.8586$ ). Due to the high number of cases with no density value, creates a variable dichotomized, indicating the presence of nerve fibers. Chi-square test detected a significant difference.

**Conclusion:** A significant difference was detected between the density of nerve fibers found in endometrial biopsies from patients with endometriosis and from patients without. It detected a statistically significant association between the presence of nerve fibers and the diagnosis of endometriosis. The detection of these fibers are useful in the diagnosis.

**Keywords:** Endometrium Nerve fibers

## Poster - Endometrium

P-62

### MATERNAL MALNUTRITION ALTERS UTERINE STRUCTURE AND REDUCES ITS CAPACITY IN THE RESULTING FEMALE OFFSPRING.

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**Objectives:** Organogenesis is a critical developmental process. Among factors that affect organogenesis is maternal malnutrition (MMn). MMn has been repeatedly reported to program offspring heart and kidney causing hypertension. Little is known about MMn effects on female reproductive system. We hypothesize that MMn alters offspring uterine structure and reduces endometrium efficiency.

**Design:** Experimental Wistar rat model was applied.

**Materials and Methods:** Pregnant rats were fed ad libitum (control) or 50% of ad libitum (MMn) throughout pregnancy. Uterus of female offspring was examined at week 4 of age. In a subgroup, female offspring were mated at week 12 of age and killed at day 20 of pregnancy to collect placenta and foetuses.

**Results:** Uterus/body weight ratio of MMn was smaller than control in all ages. Estimation of endometrium volume, using Cavalieri method, showed a significant reduction in MMn by 17%. Placenta weight was not affected but placental surface was significantly decreased in MMn. Fetus number and total weight was also decreased. Control MMn Uterus relative weight  $2.4 \pm 0.6$   $2.0 \pm 0.2$  Litter size  $12.4 \pm 1.93$   $10.3 \pm 2.12^*$  Foetuses total weight (g)  $71.9 \pm 3.1$   $54.33 \pm 0.04^*$  fetal weight/placental weight (%)  $5.3 \pm 0.30$   $4.5 \pm 0.35^*$  Placental surface

**Conclusion:** MMn programmed uterus in female offspring and reduced its capacity of producing normal litter size and weight. Placenta of MMn foetuses was unable to extend their exchange surface despite having same tissue mass. These could be linked to poor endometrium structure reflected by its small volume and maybe reduced vesiculations.

**Keywords:** Organogenesis

## Poster - Endometrium

P-63

### MATERNAL MALNUTRITION PROGRAMMES REPRODUCTIVE SYSTEM IN FEMALE RAT OFFSPRING OF FIRST AND SECOND GENERATIONS.

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**Objectives:** Maternal malnutrition during pregnancy alters fetal organogenesis. Available nutrients are redirected to the most important organs at critical times, brain and heart, in the price of less important organs such as reproductive system. It is, therefore, hypothesized that fetal uterine structure are subject to maternal malnutrition.

**Design:** Experimental Wistar rat model was applied.

**Materials and Methods:** Pregnant rats were fed ad libitum (control) or 50% in the first (F1) and second generation (F2) throughout pregnancy. Uterus was prepared for histological and stereological studies at 4 weeks of age. Subgroups were mated to investigate effects on litter size, pup's weight and pregnancy length.

**Results:** Uterus:body weight ratio was reduced in both F1 and F2 (table). Litter size was smaller in F2 than C and F1. Pup's weight was significantly reduced in both generations, however, it was smaller in F1 compared to F2. Gestation length was reduced in F2 but not F1. Uterine gland number was smaller in F2 compared to C and F1. Control F1 F2 Uterus relative weight at day 1 of age  $2.4 \pm 0.6$   $2.0 \pm 0.2^*$   $2.1 \pm 0.4^*$  Litter size  $12.4 \pm 1.93$   $12.6 \pm 1.82$   $8.7 \pm 1.04^*$  Pup weight at delivery (g)  $6.32 \pm 0.9$   $5.3 \pm 0.04^{*+}$   $5.92 \pm 0.07^*$  Gestation length (day)  $22.12 \pm 0.6$   $21.91 \pm 0.4$   $21.24 \pm 0.9^*$

**Conclusion:** Maternal malnutrition programs uterus in offspring of first and second generation. F1 and F2 female had small uterus and produced small babies. F2 may have learnt from their experience and compensated by reducing pup number and increasing birth weight. Another possible explanation is that they had less fewer uterine glands.

**Keywords:** Endometrium, Fetal Programming

## Poster - Epidemiology

P-64

### THE IMPACT OF JAPAN ENLIGHTENEMENT COMMITTEE IN ENDOMETRIOSIS (JECIE) ACTIVITIES: A PRELIMINARY REPORT

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**Objectives:** Japan Enlightenment Committee in Endometriosis (JECIE) is a non-governmental organization established in 2012, aiming to increase public awareness of endometriosis in Japan. This report will introduce the activity of JECIE projects and show its preliminary impact on the number of women who visited medical institutions for seeking management of endometriosis.

**Design:** JECIE projects contain giving lectures to various health advisers such as nursing teachers by gynecologists, leafleting, pressing, broadcasting, and establishing information stations using a website and social-networking systems. The targets of these projects are prioritized as company employees (both men and women), college students and high-school students and their mothers.

**Materials and Methods:** The numbers of patients who visited medical institutions for management of endometriosis/dysmenorrhea, and prescribed medications for endometriosis/dysmenorrhea were determined according to the Japanese National Health Insurance database. The annual increasing rate of 2012/2011 was compared with that of 2011/2010.

**Results:** The number of patients who visited medical institutions for treatment of endometriosis/dysmenorrhea during 2012 was 931,700. The annual increasing rate of 2012/2011 was 19.9%, which is significantly higher than that of 2011/2010 (6.1%). Low dose estro-progestin (LEP) was the most commonly prescribed medication for endometriosis/dysmenorrhea. The number of LEP prescription increased by 11.1% for endometriosis and by 21.6% for dysmenorrhea compared with the previous year. The number of NSAIDs prescription for endometriosis decreased by 2.5%, and that of dienogest increased by 18.4% compared with the previous year.

**Conclusion:** The number of patients who sought medical consultations for endometriosis/dysmenorrhea increased in one year after the launch of JECIE activity. Further studies are needed to clarify effective initiatives for boosting public awareness of endometriosis and motivating women to seek medical attentions.

**Keywords:** JECIE, Endometriosis, Dysmenorrhea

## Poster - Epidemiology

P-65

### THE COST OF ENDOMETRIOSIS IN AUSTRALIA

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**Objectives:** This study estimates the cost of endometriosis in Australia. It is estimated that 560,000 reproductive-aged women are affected by endometriosis. Endometriosis is frequently associated with decreased health-related, Quality of Life (HRQoL), increased chronic pain and pain-associated distress. Decreased HRQoL and increased pain is associated with rising health costs to society.

**Design:** This epidemiological study surveyed electronically available data to explore direct healthcare and indirect costs associated with endometriosis. These costs may be directly borne by the healthcare budget, government subsidies, private health insurance, employers and individuals or households. Indirect costs are often met by support organisations, familial and social networks.

**Materials and Methods:** This study was conducted by extrapolating European and North American cost-of-illness study outcomes to Australian healthcare data. This data was collected by interrogating the Australian Bureau of Statistics website for population data and the Australian Institute of Health and Welfare website for Australian Hospital Statistics 2010-2011 and Chronic Disease Statistics.

**Results:** This study suggests that endometriosis costs Australian society \$7.7 billion annually. Approximately two thirds of these costs are attributed to loss in productivity, with the remainder – about \$2.5 billion - being direct healthcare costs. Comparatively, diabetes costs about \$1 billion annually in direct healthcare costs and is identified as one of the twelve most burdensome chronic conditions in Australia. Chronic pain is also burdensome; costing about \$34 billion annually or \$11,000 per person with chronic pain. By comparison, the overall cost of endometriosis per woman is approximately \$13,000 annually. These costs may be met by a combination of funding mechanisms; both government and private.

**Conclusion:** Detailing the burden of endometriosis from a cost perspective is an important tool in optimising funding allocation and government support. In Australia, available data strongly suggests that endometriosis adds a significant, 'silent' burden to the nation's budget. A cost-of-illness study in Australia is a key area for future research.

**Keywords:** Australia, cost-of-illness, endometriosis

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### PREVALENCE OF DIAGNOSED ENDOMETRIOSIS AND SYMPTOMS BURDEN: ESTIMATES FROM A LARGE US POPULATION SAMPLE

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**Objectives:** Current literature reports a significant proportion (~10%) of pre-menopausal women experience endometriosis. Data, however, on prevalence of diagnosed endometriosis and associated symptoms is limited. In this study, we sought to estimate the prevalence of endometriosis among pre-menopausal women in the United States and to evaluate their symptom profile.

**Design:** A cross-sectional online survey of pre-menopausal US women between 18 and 54 years old was conducted by Harris Interactive between August and September 2012.

**Materials and Methods:** Data collected from women who completed the survey included demographics, age at diagnosis, history of symptoms experienced and recent symptom experience and severity. Descriptive statistics were used to report means and proportions. National estimates were derived using sampling weights computed for each individual based on age group.

**Results:** Among the 48,020 respondents aged 18-49 years, 2,922 women reported a diagnosis of endometriosis (6.1%, 95% CI: 5.8-6.4%) which projects to an estimated 4,112,049 women in the US. Mean age of patients with endometriosis was 37.8 years. The average age at diagnosis was 27 years. Prevalence was highest in patients aged 45-49 (10.0%, 95% CI: 9.0-10.9%). In the prior 4-weeks, 1,481 patients experienced menstrual associated pelvic pain (52.7%, of whom 34.4% had severe presentation), 982 experienced non-menstrual pelvic pain (36.7%, among which 17.8% had severe presentation) and 835 patients experienced dyspareunia (29.5% among which 18.2% had severe presentation). Additionally, menstrual pelvic pain, non-menstrual pelvic pain and dyspareunia were rated as extremely bothersome by 44.3%, 30.6%, and 41.8% of patients, respectively.

**Conclusion:** Endometriosis is a prevalent condition among pre-menopausal women with a large percentage continuing to suffer from severe and bothersome symptoms for years following diagnosis. These data highlight the need for an effective treatment aimed at chronic relief from endometriosis-related symptoms.

**Keywords:** Symptoms burden, severity

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### DELAYS IN ESTABLISHING ENDOMETRIOSIS DIAGNOSIS AMONG US WOMEN

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**Objectives:** Despite the importance of early diagnosis of endometriosis, studies have reported considerable delay between symptom onset and diagnosis. The purpose of this research was to quantify this delay in a sample of endometriosis patients in the United States (US) and identify stages of the diagnostic process at which delay occurs.

**Design:** A cross-sectional study of an online panel of premenopausal women in the US using a self-administered online survey completed in the period between August and September 2012.

**Materials and Methods:** The web based survey was conducted among US women aged 18-54. Endometriosis diagnosis was ascertained by patients' self-report. Delays between symptom onset and first physician visit, report of symptom to a physician and establishing diagnosis, as well as factors associated with the diagnostic delay were examined.

**Results:** 772 endometriosis-diagnosed women, aged 18-49, , completed questions regarding diagnostic delay. Mean delay between first symptom experience and first physician contact was 32 months, which was longer for patients with current age 45-49 compared to patients aged 18-29 (42 vs. 21 months, p-value <0.01), as well as patients who had symptom onset at age ≤19 compared to patients aged >19 (43 vs. 23 months, p <0.001). Mean delay from first physician visit to diagnosis was 28 months. This delay was longer for patients diagnosed surgically vs. patients diagnosed non-surgically (33 months vs. 22 months, p=0.063) and patients who had symptom onset at age ≤19 compared to patients aged >19 (37 vs. 20 months, p <0.001).

**Conclusion:** Significant delays exist in establishing an endometriosis diagnosis. It is equally driven by patients delay in seeking care and physician delay in confirming the diagnosis. Strategies to increase disease awareness may help shorten this delay

**Keywords:** diagnostic Delay

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### CLINICAL AND ALGIC CHARACTERISTICS OF WOMEN WITH ENDOMETRIOSIS AND CHRONIC PELVIC PAIN

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**Objectives:** To evaluate the clinical conditions of the patients with endometriosis.

**Design:** An epidemiological (cohort study) study was performed in the Hospital de Clínicas de Porto Alegre including 110 patients with endometriosis diagnosed by surgical procedures.

**Materials and Methods:** We interviewed our patients and clarified some aspects of their medical history. The pain was measured by the Visual-Analogue Scale (VAS – 0-10). Moreover, several demographic and physical/medical variables were collected during the interview.

**Results:** Body Mass Index (kg/m<sup>2</sup>) was higher than 25 kg/m<sup>2</sup> in 71.7% of the patients. Dysmenorrhea was present in 89.1% of the patients (VAS 7.53±3.26 for 12.52±11.09 years), dyspareunia in 70.1% (VAS 4.55±3.57 for 5.87±7.76 years), and chronic pelvic pain in 92% (VAS 6.55±2.94 for 9.1±9.42 years). For the treatment, about 18% of the women had used intrauterine device (63% of them reported decreased pain), 53% progesterone capsules (51% of them reported decreased pain), 66% oral contraceptive (43% of them showed improvement in pain), and 92% used painkillers (78% of them reported decreased pain). The average time between onset of symptoms and diagnosis was 4.83±5.65 years, and the mean age of onset of symptoms was 26.5±11.97 years. Almost 80% of the women reported social absenteeism.

**Conclusion:** This study shows that women with endometriosis have a poorer quality of life, assuming they suffer from chronic pelvic pain, dyspareunia and dysmenorrhea, besides the discomfort caused by surgeries and overweight. There is a huge interval between the onset of symptoms and the diagnosis, and no treatment is highly effective.

**Keywords:** Endometriosis; ChronicPelvicPain; Epidemiology

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### THE PREVALANCE OF ENDOMETRIOSIS IN WOMEN WHO HAD GYNECOLOGIC LAPAROSCOPY AT A UNIVERSITY HOSPITAL IN SAUDI ARABIA

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**Objectives:** To determine the prevalence of endometriosis in women who had gynecologic laparoscopy at a university hospital in Saudi Arabia.

**Design:** A retrospective observational cohort study.

**Materials and Methods:** The hospital records at King Abdulaziz University Hospital, Jeddah, Saudi Arabia were reviewed to identify all women who underwent gynecological laparoscopy at the hospital from January 2008 till December 2013. Demographic data, indications of laparoscopy, diagnosis, and operations performed were determined.

**Results:** During the study period, 190 gynecologic laparoscopies were performed. The age was  $33.8 \pm 8.9$  (mean  $\pm$  SD). The indications for laparoscopy were 76 (40%) for infertility, 34 (17.9%) for chronic pelvic pain, 7 (3.7%) for infertility and chronic pelvic pain, 30 (15.8%) for ectopic pregnancy, 12 (6.3%) for pelvic mass, 6 (3.2%) for removal of missing intrauterine contraceptive device and 25 (13.1%) for other indications. There were 21 (11.1%) women who were diagnosed with endometriosis. The presenting complaints in the 21 women with endometriosis were pelvic pain 7 (33.3%), infertility 5 (23.8%), pelvic pain and infertility 6 (28.6%), and pelvic mass 2 (9.5%) and unknown 1 (4.8%). Diagnostic laparoscopy was done in 93 (48.9%) women and operative laparoscopy was done in 97 (51.1%) women.

**Conclusion:** The diagnosis of endometriosis was not common in our cohort of women who had gynecologic laparoscopy

**Keywords:** Endometriosis, Saudi Arabia

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### COMPARATIVE ANALYSIS OF THE PREVALENCE OF ENDOMETRIOSIS ON STATE OF TOCANTINS IN RELATION TO NORTHERN REGION AND BRAZIL FOR THE PERIOD OF 2008 TO 2012

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**Objectives:** Report the prevalence of endometriosis in the state of Tocantins and compare this with the situation in the Northern Region in which is inserted and data relating to Brazil in the period 2008-2012.

**Design:** Epidemiological study, descriptive, cross-cut, with quantitative approach.

**Materials and Methods:** They were collected all of data from hospitalizations for endometriosis, available at the Department of Informatics of the Unified Health System (DATASUS) for the State of Tocantins, Northern Region and Brazil, between 2008 and 2012, assessing absolute value, age and race/color.

**Results:** There were in the state of Tocantins 1.037 cases of endometriosis, especially the city of Porto Nacional with 709 (68.37%) cases. In the Northern Region have registered 3.664 cases, with emphasis on the state of Pará (1.095-29.9%), followed by Amazonas (1.082-29.5%) and Tocantins (28.3%). In Brazil have registered 76.307 cases appearing Southeast Region first with 42.5% of cases (32.455) and the Northern Region in the latter (4.8%). The states with the highest prevalence were São Paulo, Minas Gerais and Rio de Janeiro, with the Tocantins in 18th position. In the national, regional and state sphere the age group most affected was between 40-49 years (44,16%; 37,55%; 49,18%). However, while the color/race more prevalent for Tocantins and Northern Region was mulatto, for Brazil was white.

**Conclusion:** It was concluded that endometriosis is very prevalent in Brazil and that the Northern Region and the State of Tocantins contribute little to the total cases. Therefore, it is necessary epidemiological and clinical studies more consistent that help to further elucidate the profile of patients with endometriosis.

**Keywords:** Endometriosis. Epidemiology. Brazil.

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### CLINICAL AND BIOCHEMICAL FEATURES OF INFERTILE FEMALE WITH PELVIC ENDOMETRIOSIS. A BRAZILIAN POPULATION.

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**Objectives:** To verified the clinical and bichemical features of Brazilian infertile female with pelvic endometriosis.

**Design:** Cross-sectional study including 276 patients.

**Materials and Methods:** This study was performed at the Tropical Institute of Reproductive Medicine and Menopause, Brazil. The evaluation of all patients included routine screening for female infertility and laparoscopy. Biochemical evaluation included the measurement of CA 125, thyroid hormones, gonadotropins and estradiol. Statistical analysis was performed using the SPSS software, version 18.

**Results:** The mean age was 31.72 years IC 95% ( 31.1 – 32.2); the married duration was of 7 (6.9 – 7.84) years with 3.52 (3.16 – 3.87) years without contraception. Primary infertility was found in 68.9% and secondary infertility in 31.1%. The major clinical findings were dysmenorrhea (68.9%), diarrhea/increased peristalsis (37.3%), dyspareunia (22.4%). The mean CA125 levels were 18.8 (20.6 – 30.8), estradiol 58.3 (51.5 – 65.2), LH 5.9 (6.6 – 8.6), FSH 6.7 (6.2 – 7.2), TSH 2.0 (1.8 – 2.2), free T4 1.4 (1.2 – 1.8).

**Conclusion:** The Brazilian infertile patients with pelvic endometriosis had more than two years of infertility before complete investigation. Most of them present dysmenorrhea and near 40% presented increased peristalsis/diarrhea. The levels of CA 125 were not increased in this population.

**Keywords:** Infertility, endometriosis, epidemiology

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### PRELIMINARY DATA OF THREE YEARS OF ENDOMETRIOSIS BOWEL TREATMENT IN A SINGLE CENTER

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**Objectives:** Endometriosis bowel treatment still has no consensus nowadays. Several authors defend the systematic use of bowel resection while others give preference to bowel shaving. Our objective is to review the outcomes of patients treated for bowel endometriosis: pain and bowel symptoms, functional symptoms, complications, recurrences and pregnancy rate

**Design:** Retrospective review of outcomes of patients treated for bowel endometriosis

**Materials and Methods:** Patients that underwent surgery between January 2010 and September 2013 for bowel shaving, discoid resection, segmental bowel resection, appendectomy, caecal partial resection.

**Results:** According to the type of surgery performed, we intend to describe the size of the specimen extracted, pain and bowel symptoms (dysmenorrhea, dyspareunia, chronic pelvic pain, dysuria, dyschesia, constipation, diarrhea and rectorragia), functional symptoms (bladder and bowel), complications (intraoperative and post operative), endometriosis bowel recurrences, pregnancy rates and general outcomes.

**Conclusion:** In our group we give preference to treat the bowel endometriosis according to the patient's symptomatology, disease location (rectal vs sigmoid), nodule size, multifocal disease and bowel stenosis.

**Keywords:** Bowel Endometriosis Treatment

Poster - Genetics, epigenetics and hereditary aspects

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**EXPRESSION PROFILE OF HISTONE METHYLTRANSFERASES (HMT'S) IN ENDOMETRIOSIS**

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**Objectives:** To assess expression levels of histone methyltransferases (HMTs) and determine whether histone methylation marks may play a role in regulation of transcription in endometriosis. We hypothesized that endometriotic cell lines and tissues will have characteristic profiles of HMTs and of histone methylation marks in promoter regions of candidate genes.

**Design:** In vitro studies to determine histone methyltransferases protein expression.

**Materials and Methods:** Western blot (WB) was conducted to assess HMTs protein levels. To determine whether candidate genes are regulated by histone marks in lesions vs. control endometrium, chromatin immunoprecipitation (ChIP)-PCR and qPCR will be conducted.

**Results:** WB showed a different pattern of HMT protein expression among the cells studied. SET-1 and SET-9 were expressed in 12Z (epithelial endometriotic) and in stromal primary endometriotic cell lines (sPEC). SETDB1 was expressed exclusively in sPEC. We have previously conducted bioinformatic analyses to identify areas of enrichment for H3K4me, H3K27me and H3K9me in promoter regions of ESR1, CDH1, p21, SF1, and HOXA10, which are also enriched for histone acetylation marks (e.g., H3K4ac, H3K9ac) (Monteiro et al, 2013). Primers for ChIP-PCR were designed and experimentally tested. Ongoing studies includes ChIP-PCR for candidate genes in lesions and endometrium from patients and controls) using antibodies to H3K4me3, H3K27me3 and H3K9me3; validation of WB results by IHC; and regulation of HMT expression by steroid hormones in cell lines.

**Conclusion:** These studies will help understand the regulatory role that HMTs may exert on the transcription of candidate genes in endometriosis. Elucidating the expression profile and function of HMTs in endometriosis may support the use of novel treatments that target the epigenetic component of this enigmatic disease

**Keywords:** Endometriosis, Epigenetics, Histone-methyltransferases

Poster - Genetics, epigenetics and hereditary aspects

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**COMPLEX INTERACTIONS BETWEEN FOXL2, DLX5 AND DLX6 AND ROLE IN ENDOMETRIOSIS PATHOGENESIS: RESULTS OF A PRELIMINARY STUDY**

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**Objectives:** Endometriosis shows complex hormonal deregulations in both eutopic and ectopic endometrium. FOXL2, DLX5 and DLX6 are transcription factors involved in steroidogenesis. They are highly expressed in the endometrium and deregulated in endometrioma. We aimed to evaluate the role of these genes and their mutual interactions in this context

**Design:** Functional laboratory study on cell cultures

**Materials and Methods:** Five patients operated for complete treatment of symptomatic endometriosis were recruited. Samples of eutopic and ectopic endometrium were obtained and cultured after separation of stromal and epithelial cells. Expression of FOXL2, DLX5, DLX6 was studied by qPCR in each cell population with and without inhibition by the corresponding siRNA.

**Results:** FOXL2 was expressed predominantly in the eutopic endometrial cells (stromal or epithelial). DLX5 and DLX6 were mainly expressed in epithelial cells of the endometrium. For all patients, we observed a decreased expression of DLX5, DLX6 and FOXL2 in the lesions. Blocking FOXL2 by siRNA resulted in an induction of DLX5 in the lesions (both epithelial and stromal cells) and an induction of DLX6 in stromal cells of the eutopic endometrium. On the contrary, inhibiting the expression of DLX5 produced a decrease of the expression of FOXL2 in the eutopic endometrium (both epithelial and stromal cells), while that of DLX6 decreased in the epithelial cells of the endometrium and increased in epithelial cells the lesion

**Conclusion:** There is a complex interaction between DLX5, DLX6 and FOXL2 in endometriosis, whose nature depends on the tissue (eutopic and ectopic endometrium) but also on the cell population (epithelial or stromal cells). This preliminary study required confirmation on larger populations

**Keywords:** Dlx5, dlx6, foxl2

Poster - Genetics, epigenetics and hereditary aspects

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**MICRORNA REGULATION OF PAIN ASSOCIATED WITH ENDOMETRIOSIS**

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**Objectives:** Chronic pain is one of the major symptoms associated with endometriosis. The etiology of this pain is still unknown. One of the recent theories is a role for epigenetics (including microRNA) in pain. The objective of this study was to determine the regulatory role of microRNAs in pain in endometriosis.

**Design:** Whole-genome human microne and differential expression of human nociceptive and inflammatory genes were performed in peritoneal or ovarian endometriotic tissues obtained from IRB approved and consented patients with +endometriosis/+pain, +endometriosis/-pain, and -endometriosis/-pain. Ingenuity pathway analysis and Targetscan was used for bioinformatics analysis of the differential expressed microRNAs and target genes.

**Materials and Methods:** MicroRNA was isolated using miRNeasy kits from endometriotic tissues from all groups of patients. After purity and integrity were analyzed using NanoChip, samples were used for whole-genome human microne PCR array. The tissue RNA was used for determining the target nociceptive genes by the Human pain: Nociceptive and Inflammatory array.

**Results:** Statistical and Bioinformatics approach of the whole-genome microne array determined microRNAs that were differentially expressed between patients who had pain versus controls who did not have pain. MicroRNAs such as let-7i, 7g, miR-24, miR-29a, miR-26b, miR-148a that target DNA methylases 1 and 3, BCL2, opioid receptors, interleukin-6 receptor, prostaglandin receptor 4 etc, were upregulated, whereas miR-548, miR-518, miR-1538 etc, that target opioid receptors and other inflammatory genes were downregulated in patients with pain compared to controls. Human pain array revealed differential expression of genes involved in nociceptive pathways such as interleukins, prostaglandin receptors, voltage-gated sodium channel genes and opioid receptors in patients with pain compared to controls.

**Conclusion:** Our studies suggest a regulatory role for microRNAs in pain associated with endometriosis. The differentially expressed microRNAs target not only inflammatory and nociceptive genes but also other epigenetic genes such as DNA-methylases. Validation of these target genes and their association with pain in endometriosis will identify potential targets for therapy.

**Keywords:** MicroRNA, Endometriosis, pain

**Poster - Genetics, epigenetics and hereditary aspects**

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**FIBRINOLYTIC SYSTEM GENE POLYMORPHISMS AND ENDOMETRIOSIS RISK**

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**Objectives:** To examine single gene polymorphisms (SNPs) in the inhibitors of fibrinolysis, i.e. the plasminogen activator inhibitor type 1 (PAI-1), and tissue activatable fibrinolysis inhibitor (TAFI), and stimulators of fibrinolysis, i.e. tissue (tPA) and urokinase (uPA) plasminogen activator genes, in endometriosis cases and controls.

**Design:** A total of 840 patients (328 laparoscopically diagnosed endometriosis cases and 512 controls) were recruited for this study from 2 populations; a case-control study (122 endometriosis cases and 90 controls; study I) and a nested case-control study from NHS II (206 endometriosis cases and 422 controls; study II).

**Materials and Methods:** Blood samples were collected from all subjects. DNA extraction was performed. A total of 16 SNPs in the promoter regions of the 4 genes thought to be associated with fibrinolysis were genotyped by Polymerase chain reaction in study I or sequenced in study II.

**Results:** The insertion deletion SNP (rs1799768) on the promoter region of PAI-1 was significantly associated with endometriosis in study I. However, we did not find a statistically significant difference in the distribution of the tested SNPs in the promoter regions of TAFI, UPA and tPA genotypes between the 2 groups in the 2 studies independently or in combined analyses.

**Conclusion:** Single gene polymorphisms in the principal inhibitor of fibrinolysis (PAI-1) was associated with laparoscopically-confirmed endometriosis. The association of this particularly SNP with hypofibrinolysis may contribute to disordered clearance of fibrin at the time of retrograde menstruation and predispose to disease initiation or recurrence.

**Keywords:** fibrinolysis, PAI-1, TAFI, uPA, tPA.

Poster - Genetics, epigenetics and hereditary aspects

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**DEATH RECEPTOR 6 IS EPIGENETICALLY SILENCED BY HISTONE DEACETYLATION IN ENDOMETRIOSIS AND PROMOTES PATHOGENESIS OF ENDOMETRIOSIS**

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**Objectives:** Accumulating evidences suggest that various epigenetic aberrations play definite roles in the pathogenesis of endometriosis. Aberrant expression of histone deacetylases has been demonstrated in endometriosis. The purpose of this study is to evaluate the role of epigenetically silenced genes in the pathogenesis of endometriosis.

**Design:** This study was designed to identify (1) the panel of the tumor necrosis factor receptor superfamily genes that are aberrantly repressed in endometriotic stromal cells by histone acetylation and (2) the functions of death receptor (DR) 6, an epigenetically repressed molecule in endometriotic stromal cells, in the pathogenesis of endometriosis.

**Materials and Methods:** The effect of valproic acid on the DR6 expression in endometriotic stromal cells was examined. The roles of DR6 in eutopic endometrial stromal cells were investigated with DR6 siRNA transfection. The expression of DR6 mRNA and protein in endometriotic stromal cells and eutopic endometrial stromal cells were also examined.

**Results:** Among the tumor necrosis factor receptor superfamily mRNAs including DR1, DR2, DR3, DR4, DR5, DR6, ectodysplasin A receptor, and nerve growth factor receptor, we found that only DR6 mRNA was significantly upregulated in the valproic acid-treated endometriotic stromal cells compared to the untreated endometriotic stromal cells by using a global microarray technique. DR6 mRNA and protein expression was attenuated in cultured endometriotic stromal cells and in endometriotic tissues, and its expression was upregulated by valproic acid stimulation. Chromatin immunoprecipitation assays revealed an accumulation of acetylated histone H4 in the promoter region of the DR6 gene by valproic acid treatment. DR6 knockdown directed the stimulation of cell proliferation and the resistance to apoptosis in eutopic endometrial stromal cells.

**Conclusion:** It is suggested that DR6 is involved in the pathogenesis of endometriosis by creating the proliferative and anti-apoptotic characteristics of endometriosis. The results also suggest that histone deacetylase inhibitors are promising agents for the treatment of endometriosis. Further research with epigenetically silenced genes in endometriosis may elucidate its pathogenesis.

**Keywords:** Death receptor, apoptosis

Poster - Genetics, epigenetics and hereditary aspects

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**LYSINE-SPECIFIC DEMETHYLASE 1 (LSD1) IS A POTENTIAL MOLECULAR TARGET FOR ENDOMETRIOSIS**

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**Objectives:** We sought to investigate as whether LSD1 is aberrantly expressed in endometriosis, and, if so, treatment with tranilcypromine, an LSD1 inhibitor, have any effect on cell viability, cell cycle, and invasiveness. In addition, we sought to determine whether treatment with tranilcypromine have any therapeutic value for mice with induced endometriosis.

**Design:** Cross-sectional clinical studies of women with and without endometriosis, lab investigation, and an animal experiment evaluating the potential therapeutic efficacy of LSD1 inhibitor tranilcypromine (TC).

**Materials and Methods:** Immunohistochemistry analysis of ectopic/eutopic endometrial tissues from women with and without endometriosis; gene expression and protein analysis using primary endometriotic stromal cells (EESCs) and normal endometrial stromal cells (NESCs) were used. Mouse experiments were conducted to examine the therapeutic efficacy of TC to treat endometriosis in mice with induced endometriosis.

**Results:** LSD1 gene and protein expression in ectopic endometrium was significantly elevated as compared with normal endometrium. Treatment of endometriotic stromal cells with tranilcypromine significantly reduced cellular proliferation, cell cycle progression, and invasiveness. Treatment with tranilcypromine results in markedly reduced lesion size and improved hyperalgesia in mice with induced endometriosis, along with reduced MVD and immunoreactivity to PCNA, VEGF, and vimentin but increased immunoreactivity to E-cadherin, H3K4me1 and H3K4me2.

**Conclusion:** Since DNA and histones are intimately intertwined and work in concert in transcription regulation, histone demethylation activity of LSD1 could be wide-ranging. The inhibition of LSD1 activity by tranilcypromine resulted in desirable effect in vitro and in vivo, suggesting that LSD1 may be a candidate therapeutic target for endometriosis.

**Keywords:** Endometriosis, LSD1, MAOI

Poster - Genetics, epigenetics and hereditary aspects

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**PLASMINOGEN ACTIVATOR INHIBITOR 1 4G5G POLYMORPHISM IN INFERTILE WOMEN WITH AND WITHOUT ENDOMETRIOSIS**

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**Objectives:** The objective of this study was to evaluate the genotypes of the plasminogen activator inhibitor gene pai-1 in a group of infertile women with and without endometriosis and a control group.

**Design:** Prospective case-control study in a university human reproductive service

**Materials and Methods:** A case-control study was conducted in the human reproduction center of the faculty of medicine of abc with 140 infertile women with endometriosis, 64 women with idiopathic infertility and 148 fertile women as a control group. The 4g/5g polymorphism of pai-1 gene was identified by polymerase chain reaction of restriction fragments.

**Results:** THE FREQUENCY OF THE GENOTYPES 4G/4G, 4G/5G and 5G/5G PAI-1 GENE IN INFERTILE WOMEN WITH ENDOMETRIOSIS WERE 38.6%, 37.1 AND 24.3, RESPECTIVELY, AND THE CONTROL GROUP OF 24.3, 33.8 AND 41.9%, RESPECTIVELY ( $p = 0.003$ ). WHEN INFERTILE WOMEN WITH ENDOMETRIOSIS WERE DIVIDED ACCORDING TO THEIR STAGES OF ENDOMETRIOSIS GENOTYPES 4G/4G, 4G/5G AND 5G/5G WERE IDENTIFIED, RESPECTIVELY, 36.7, 32.9 AND 30.4% OF PATIENTS WITH ENDOMETRIOSIS MINIMAL / MILD ( $p = 0.102$ ) AND 41.0, 42.6 AND 16.4% OF PATIENTS WITH MODERATE / SEVERE ( $p = 0.001$ ) IN WOMEN WITH IDIOPATHIC INFERTILITY, THE GENOTYPES WERE FOUND AT A FREQUENCY OF 29, 34.3 AND 36%, RESPECTIVELY ( $p = 0.637$ ).

**Conclusion:** These data suggest that in Brazilian women the pai-1 4g/5g polymorphism may be associated with a risk of infertility associated with endometriosis and also may collaborate for the evolution of the condition to more severe stages

**Keywords:** Pai-1, infertility, endometriosis

Poster - Genetics, epigenetics and hereditary aspects

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**ENDOMETRIAL PROTEIN EXPRESSION STUDIES OF GENES IDENTIFIED BY GENOME WIDE ASSOCIATION STUDIES (GWAS) THAT MAY CONFER INCREASED RISK FOR SUSCEPTIBILITY TO ENDOMETRIOSIS.**

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**Objectives:** To examine protein expression of endometriosis risk genes from endometrium collected from women homozygous and heterozygous for endometriosis risk alleles.

**Design:** Women undergoing laparoscopy at the Royal Woman's Hospital (Melbourne) were recruited for this study. A questionnaire, blood sample and eutopic endometrium were collected.

**Materials and Methods:** Blood samples were genotyped and subsequently women were categorised as homogeneous for the risk allele (RA), homogeneous for the other allele (OA) or heterogeneous (Het.). Expression of Wnt4 and VEZT were investigated by immunohistochemistry (IHC) and Western blot.

**Results:** Immunoreactive Wnt4 was present in the glandular epithelium and stroma of the endometrium. Expression is mainly cytosolic. Quantitative analysis of the Western blot 39kDa band from RA (n=5), OA (n=26) and Het. (n=14) women did not demonstrate any differential expression of Wnt4 protein. VEZT protein was expressed in the glandular epithelium and was largely restricted to the cytosol. Western blot analysis of the 89kDa band from RA (n=8), OA (n=26) and Het. (n=22) women did not demonstrate any differential expression of VEZT protein.

**Conclusion:** Neither Wnt4 nor VEZT showed differential expression between women homozygous for risk alleles or other alleles. Further investigation of expression patterns of additional genes are required to develop insights into the functionality of endometriosis risk alleles identified by GWAS.

**Keywords:** Endometriosis, gene, risk

**Poster - Genetics, epigenetics and hereditary aspects**

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**COPY NUMBER VARIATION IN PELVIC ENDOMETRIOSIS.**

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**Objectives:** Endometriosis is one of the most common gynecologic disorders affecting, 2-22% of women of reproductive age. Despite extensive research of endometriosis including genetic studies, the etiology and pathogenesis are quite limited.

**Design:** This study was designed for identification and validation of copy number variation (CNV) in patients with pelvic endometriosis.

**Materials and Methods:** I genotyped subjects (65 cases and 673 matched controls with no pelvic endometriosis) for CNV screening on Affimatrix SNP Chip. 41 regions were screened for candidates of CNV and analyzed statistically by multiple logistic regression analysis. Real-time quantitative PCR (qPCR) was used for confirmation of candidate.

**Results:** Association analysis was performed on 41 CNV regions (CNVR). Two CNVRs were identified with significant difference between the endometriosis and control group ( $P < 0.05$ ). CNVR of 1q21.3 did not contain any coding gene and showed significantly lower incidence of copy number losses in the endometriosis group compared to controls ( $p < 0.028$ ). CNVR of 1p13.3 was coding glutathione S-transferase M1 (GSTM1), and showed much higher copy number gain CNVs in the endometriosis group compared to controls ( $p < 0.038$ ). Genomic qPCR showed significantly less deletion of CNV in the endometriosis group in 1q21.3 region ( $p = 0.032$ ). CNVR 1p13.3 was gained more in the group of endometriosis but there was no significance ( $p = 0.237$ ).

**Conclusion:** This study identified two CNVRs for endometriosis. 1q21.3 and 1p13.3 could be a potential target for screening and diagnosis of pelvic endometriosis

**Keywords:** endometriosis, CNV

Poster - Genetics, epigenetics and hereditary aspects

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**POLYMORPHISMS IN VASCULAR ENDOTHELIAL GROWTH FACTOR (VEGF) ARE ASSOCIATED WITH RISK (-2578C>A, -1154G>A) OR PROTECTION (405G>C) OF ENDOMETRIOSIS IN BRAZILIAN WOMEN**

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**Objectives:** To investigate the association of VEGF polymorphisms (-2578C>A, -460T>C, -1154G>A, 405G>C, 936C>T) with endometriosis in Brazilian women.

**Design:** Case control genetic association study

**Materials and Methods:** 178 women surgically diagnosed with endometriosis and 49 controls undergoing laparoscopy for the tubal ligation and without the disease were enrolled into the study. The VEGF polymorphisms were determined by TaqMan real-time polymerase chain reaction. Allele, genotype and haplotypes distribution were compared between two groups.

**Results:** Our results indicate positive associations between variant genotypes of -2578C>A and -1154G>A with endometriosis (OR: 1.95, 95% CI: 1.02 - 3.72, P = 0.041 and OR: 2.23, 95% CI: 1.08 - 4.61, P = 0.043, respectively). In contrast, variant genotypes of 405G>C are negatively associated with endometriosis (OR: 0.47, 95% CI: 0.24 - 0.94, P = 0.046). No significant difference was found in allele and genotype distributions of the -460T>C and 936C>T polymorphisms between two groups. A total of six haplotypes were inferred derived from four polymorphisms (-2578C>A, -460T>C, -1154G>A and 405G>C). There was positive association between ACAG and CTGG haplotypes with endometriosis (OR: 2.49, 95% CI: 1.29 - 4.80, P = 0.009 and OR: 1.96, 95% CI: 1.04 - 3.70, P = 0.05, respectively).

**Conclusion:** The VEGF -2578CA+AA, -1154GA+AA genotypes and ACAG, CTGG haplotypes were associated with the risk of endometriosis in Brazilian women. In contrast, the 405GC+CC genotypes may be protective against the development of endometriosis.

**Keywords:** Endometriosis; VEGF; polymorphisms

Poster - Genetics, epigenetics and hereditary aspects

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**DIRECT SEQUENCING OF DNMT3L GENE REVEALS NEW POLYMORPHISMS ASSOCIATED WITH OVARIAN ENDOMETRIOMA**

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**Objectives:** Hypermethylation of the subtelomeric regions is a hallmark of endometriosis. DNA methyltransferase 3L (DNMT3L) is a good candidate gene for epigenetic alterations since specific haplotypes have been associated with both endometriosis and methylation abnormalities at the chromosome extremities. We intended to search for coding polymorphisms of DNMT3L gene.

**Design:** Direct sequencing of DNMT3L gene in patients with and without ovarian endometrioma

**Materials and Methods:** We extracted genomic DNA from 22 individuals, 18 afflicted with isolated ovarian endometrioma who underwent complete surgery and 4 controls without endometriosis as checked surgically. We amplified DNMT3L gene by long-range PCR using specifically designed primers. We then performed DNA direct sequencing following Sanger's method

**Results:** We confirmed in all patients the presence of rs7354779, a polymorphism that was previously reported by our team as associated with endometrioma. We found two additional polymorphisms in at least 66% of the patients. The first one was located in a region upstream from exon 1 and could modify fixation of transcription factors according to THSEARCH software. The second one was located in exon 5 and could be a deleterious mutation altering protein sequence, according to POLYPHEN software predictive models.

**Conclusion:** We reported two new polymorphisms of DNMT3L gene that could modify transcription or protein structure. Further analyses of the functional consequences of these polymorphisms are needed.

**Keywords:** DNMT3L; methylation; SNP

**Poster - Genetics, epigenetics and hereditary aspects**

**P-84**

**CHANGES IN THE EXPRESSION OF THE CD63, S100A6 AND GNB2L1 GENES MAY BE INVOLVED IN ENDOMETRIOSIS.**

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**Objectives:** To analyze the expression of the CD63, GNB2L1 and S100A6 genes to better understand the molecular environment of endometriotic lesions and to elucidate the potential mechanisms that underlie the complex physiopathology of endometriosis.

**Design:** A descriptive comparative study was conducted on 15 women without a laparoscopic diagnosis of endometriosis, involving biopsies of eutopic endometrium (n = 40) and ectopic (n = 40) endometrium (20 peritoneal and 20 ovarian biopsies) obtained during the proliferative and secretory phases of the menstrual cycle.

**Materials and Methods:** Gene's expression of CD63, GNB2L1 and S100A6 was determined by real time PCR by the 2- $\Delta\Delta$ Ct method. Data were analyzed statistically comparing proliferative phase versus secretory phase, patients endometrium with endometriosis versus women's endometrium without disease, eutopic endometrium versus paired ectopic endometrium, and control endometrium versus ectopic lesion.

**Results:** Significantly higher expression of the CD63, GNB2L1 and S100A6 genes was detected in the endometriotic lesions than in the eutopic endometrium of women with and without endometriosis regardless of the phase of the menstrual cycle. A significantly higher expression of only the S100A6 gene was detected during the secretory phase in the endometrium of women without endometriosis, with no other changes being detected regarding the genes studied when the proliferative and secretory phases of the cycle were compared to one another in the different tissues.

**Conclusion:** Increased expression of CD63, S100A6 and GNB2L1 genes can lead to loss of cellular ectopic implants homeostasis, contributing to the implantation and survival of the tissue in the extrauterine environment, therefore mechanisms are involved in the extracellular matrix degradation, apoptosis reduction, and increase of angiogenesis and cell motility.

**Keywords:** Cd63, s100a6, gnb2l1

Poster - Genetics, epigenetics and hereditary aspects

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**INVOLVEMENT OF MMPS REGULATORS SPARC AND RECK (CANONICAL AND SPLICING ISOFORMS) IN ENDOMETRIOSIS**

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**Objectives:** To date, no studies are available on expression of RECK isoforms or SPARC or their correlation with other regulators in deep infiltrating endometriosis. The objective is to analyze the expression profiles of MMPs and their regulators, TIMPs, SPARC, RECK and its new isoforms, to describe their involvement in endometriosis.

**Design:** We analyze samples of eutopic and ectopic endometrium of five patients with deep infiltrating endometriosis. As normal controls, we included a pool of endometrium from healthy fertile women.

**Materials and Methods:** RRNA were extracted of each sample using Trizol and cDNAs were synthesized. Using qRT-PCR, the expression profiles of MMPs-2,-3,-7,-9,-10,-14, TIMP-1,-2,-3, SPARC, RECK and their isoforms in eutopic and ectopic endometrium were analyzed. The gene expression of ectopic endometrium was compared with a pool of endometrium from healthy fertile women (control).

**Results:** Endometriosis is a benign gynecological disorder characterized by ectopic growth of endometrial cells. The ectopic endometrium degrades the extracellular matrix (ECM), through the activity of metalloproteases (MMPs) and other molecules, and invades the surrounding tissue with corresponding cell proliferation and neoangiogenesis. Degradation of the ECM by MMPs is closely regulated by tissue inhibitors of proteases (TIMPs) under normal physiological conditions. Additional MMPs regulators are: RECK, which negatively regulates MMPs in tumors, and SPARC, which upregulates MMPs. We have recently described three new RECK gene isoforms (RECKB, RECKD, RECKI), which are modulated in glioblastoma. All genes analyzed (MMPs, TIMPs, RECKs, SPARC) were upregulated both in ectopic and eutopic endometrium, with RECKB expression being increased 3-20 fold. SPARC, RECKD and RECKI had an increase in ectopic endometrium.

**Conclusion:** Our results indicate that RECKB could be used as a marker to detect early stages of the disease in ectopic endometrium, and that new genes (SPARC and RECK and its isoforms) are involved in endometriosis.

**Keywords:** deep-infiltrating-endometriosis, RECK, biomarkers

Poster - Genetics, epigenetics and hereditary aspects

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ASSOCIATION OF GSTM1 AND GSTT1 GENES WITH ENDOMETRIOSIS IN BRAZILIAN WOMEN

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**Objectives:** To compare the frequencies of polymorphic genes GSTM1 and GSTT1 in women with and without endometriosis.

**Design:** This study design is Case-control.

**Materials and Methods:** The study involved 218 patients with or without endometriosis from the Tropical Institute of Reproductive Medicine and Menopause. and Genetic Laboratory, Federal University of Mato Grosso. Interventions performed were laparoscopic and biopsy of endometriotic lesions. The main criteria used were histopathologic confirmation of endometriosis and GSTM1 and GSTT1 genes prevalences.

**Results:** There were no differences in the frequencies of the polymorphisms of GSTM1 gene between cases and controls: OR=1.13; 95% IC: 0.656-1.93 ( $p = 0.659$ ) and GSTT1 between cases and controls: OR = 0.53; 95% IC: 0.94-0.29 ( $p = 0.039$ ). No relationship between menstrual cycle interval and frequency of GSTM1 in either cases or controls ( $p = 0.370$  and  $p = 0.664$  respectively) was found. There was no relationship between menstrual cycle interval and GSTT1 polymorphism in cases (value  $p = 0.797$ ), but in controls a  $p$  value of 0.052 was found.

**Conclusion:** The frequency of null polymorphism of GSTM1 did not show any statistically significant difference between cases and controls. The GSTT1 null genotype showed statistically significant difference, with protective effect of control in woman.

**Keywords:** Endometriosis, DNA polymorphisms

Poster - Genetics, epigenetics and hereditary aspects

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**DEVELOPMENT OF A WEB SYSTEM TO STORE, RECOVER AND COMPARE PUBLISHED  
INFORMATIONS RELATED TO GENE EXPRESSION OF ENDOMETRIOTIC PATIENTS**

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**Objectives:** Endometriosis is a gynecological disease characterized by the presence of endometrial tissue outside the uterine cavity.

**Design:** Development of a web system to store.

**Materials and Methods:** Many investigations demonstrate that there is a large complex of molecules and metabolic pathways that may be related to the etiology of endometriosis.

**Results:** Studies that aim to identify the gene expression pattern of this disease comparing different endometrial tissues in women with and without endometriosis have been published. Due to the large variation of parameters tested the results are frequently divergent among authors. To precisely infer which molecules are really involved in the role of endometriosis it is important to gather this studies, compare, analyze and relate them.

**Conclusion:** The present study presents the first system in web space capable of storing, recover, compare and relate all these results in order to collect the main data regarding the differences in gene expression in endometriosis, aiming a better comprehension of this disease's etiology.

**Keywords:** Endometriosis, web system

## Poster - Immunology and stem cells

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### INTERLEUKIN-17A EXPRESSION IN THE PLASMA AND ENDOMETRIOTIC TISSUE FROM WOMEN WITH ENDOMETRIOSIS

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**Objectives:** IL-17A is a member of pro-inflammatory cytokines implicated in the pathogenesis endometriosis but its role in disease progression is poorly understood. This study was conducted to elucidate potential involvement of IL-17A in the pathogenesis of endometriosis.

**Design:** Basic science research in a laboratory setting involving endometriosis patient and control samples.

**Materials and Methods:** IL-17A concentration was measured in plasma, eutopic, ectopic samples from endometriosis patients and in plasma and eutopic samples from control subjects. Immunohistochemistry for IL-17A was conducted on eutopic and ectopic tissue sections. Proliferation, apoptosis, supernatant cytokine analysis of endometrial-epithelial carcinoma cell line (EECC) were performed with or without IL-17 stimulation.

**Results:** Higher concentration of IL-17A was found in plasma samples and ectopic tissue samples from women with endometriosis compared to plasma samples from disease free women or matched eutopic tissue samples. Immunostaining of eutopic and ectopic tissue sections showed increased localization of IL-17A in ectopic tissues compared with eutopic endometrium. IL-17A has shown no proliferative or apoptotic effect on EECC line. However, IL-17A stimulation on EECCs significantly increased production of G-CSF, VEGF, PDGF-AA, and SDF-1 in culture supernatant samples. Using qPCR, we confirmed mRNA expression of IL-17A, IL-17RA, and IL-17RC in EECCs and primary endometrial epithelial cells.

**Conclusion:** Increased expression of IL-17A in the eutopic and ectopic tissue from endometriosis patients compared to disease free endometrium from control subjects is indicative of a potential biological role of IL-17A in the pathogenesis of endometriosis. Further analysis is under progress to elucidate how IL-17 contributes to the inflammatory process.

**Keywords:** IL-17, Endometriosis, Cytokines

## Poster - Immunology and stem cells

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### SOLUBLE HLA-G IN ENDOMETRIOSIS

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**Objectives:** Membrane HLA-G and soluble HLA-G (sHLA-G) are responsible for the inhibition and even apoptosis of natural killer (NK) cells and cytotoxic T lymphocytes. The aim of this study is to evaluate the sHLA-G levels in women in different stages of endometriosis, and to compare the levels to women without endometriosis.

**Design:** Case-control study of women with and without laparoscopic evidence of endometriosis.

**Materials and Methods:** 68 women with endometriosis confirmed by laparoscopy and histological biopsies and 37 women who underwent laparoscopic tubal ligation (control group) had serum and peritoneal fluid sHLA-G levels measured using ELISA technique (EXBIO Antibodies - BioVendor, Czech Republic) The lowest limit of detection was 3U/mL. Mann-Whitney test Statistical analysis.

**Results:** The sHLA-G levels were significantly higher in peritoneal fluid (median 25.21, 0-153.00) than in serum (median 8.50, 0-121.40) of endometriosis patients ( $p < 0,0001$ ). Similar standards were observed in control group (peritoneal fluid, median 26.86, 3.29-56.20; serum, median 6.83, 0-33.84) ( $p < 0.0001$ ). No differences were observed in sHLA-G levels in serum and peritoneal fluid between the groups. The sHLA-G levels in peritoneal fluid in the initial stages of the disease (I and II, 14.7%) ranged from 0 to 63.38 U/mL (median 19.15) and in severe endometriosis (III and IV, 85.3%) sHLA-G levels ranged from 1.43 to 153.0 U/mL (median 25.95), showing similar levels between patients with early and advanced disease ( $p =$  not significant).

**Conclusion:** Statistically significant difference in sHLA-G levels in serum and PF in both groups were not demonstrated in these preliminary results, although wider range in the endometriosis group was detected. Soluble HLA-G may be involved in reducing cytotoxic activity of NK cells, which compromises the clearance of endometriotic cells.

**Keywords:** soluble HLA-G; endometriosis

## Poster - Immunology and stem cells

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### ANTINUCLEAR ANTIBODIES IN INFERTILE PATIENTS WITH PERITONEAL ENDOMETRIOSIS

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**Objectives:** To evaluate the role of five different antibodies against extractable nuclear antigen (ENA: RNP, Scl-70, SS-B, SS-A and Sm in infertile patients with peritoneal endometriosis).

**Design:** A case-control study was designed including 43 patients with endometriosis and 46 healthy controls.

**Materials and Methods:** Patients diagnosed with infertility and peritoneal minimal/mild endometriosis (n=43) and fertile women (n=46) have had a serum sample collected. A immunofluorescence assay was performed to analyze five ENA-autoantibodies (Sm, RNP, Scl-70, SS-A, SS-B). The prevalence of autoantibodies and the intensity of immunoreactions were compared between both groups.

**Results:** Prevalence was not statistical different between case and controls for anti-ENA antibodies (20.9% x 17.4%; P=0.877); anti-RNP antibodies (2.2% x 2.3%; P=1.000); anti-SS-A antibodies (14.0% x 15.2%; P=1.000); and anti-Sm antibodies (9.3% x 2.2%; P=0.193). There were no cases demonstrating positive anti-Scl-70 or anti-SS-B antibodies in the study group. The prevalence of anti-ENA antibodies among patients with minimal endometriosis was higher, but not statistical different, in comparison with the mild endometriosis group (27.5% x 7.1%; P>0.05). The intensity of immunoreactions was similar between cases and controls for anti-RNP and anti-SS-A antibodies. However, the intensity of immunoreactions for anti-Sm antibodies was higher in the endometriosis group (16.0±10.8 x 11.7±3.4, P=0.007).

**Conclusion:** Infertile patients with minimal/mild endometriosis had higher levels of anti-Sm autoantibodies.

**Keywords:** Autoantibodies; endometriosis; autoimmune-diseases

## Poster - Immunology and stem cells

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### EVALUATION OF NATURAL KILLER T CELLS IN PATIENTS WITH RECTOSIGMOID ENDOMETRIOSIS AND CONTROL PATIENTS.

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**Objectives:** Analyze the percentage of natural killer T (NKT) cells in peripheral blood (PB) and peritoneal fluid (PF) of patients with rectosigmoid endometriosis and patients without endometriosis.

**Design:** Prospective and case control study.

**Materials and Methods:** In this study, PB and PF samples were collected from 18 patients with rectosigmoid endometriosis (group A) and 9 patients submitted to bilateral tubal occlusion without endometriosis (group B). The proportion of NKT cells and subtypes were evaluated by flow-cytometry and compared between groups. Mann-Whitney test was used for analysis.

**Results:** Samples of PB from 4 patients with endometriosis, PF samples from 5 patients with endometriosis and 3 patients without endometriosis were not viable and excluded. There was no statistical difference in NKT cells percentage in blood and peritoneal fluid samples between group A and group B. The proportion of NKT cells in PB and PF in patients with endometriosis was not statistically different. The analysis of subtypes of NKT cells (CD8+, CD4+CD8+, CD4+ and CD4-CD8-) in PB and PF in endometriosis group compared with control group also showed no statistical difference.

**Conclusion:** The percentage of NKT cells and NKT subtypes are not different in peripheral blood and peritoneal fluid in patients with rectosigmoid endometriosis when compared to patients without endometriosis. The results of this study are important to increase knowledge about the correlation of immune system and endometriosis development.

**Keywords:** Endometriosis, NKT cells.

## Poster - Immunology and stem cells

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### EVALUATION OF ANGIOGENESIS IN EXPERIMENTAL ENDOMETRIOSIS IN WISTAR RATS TREATED WITH BEVACIZUMAB

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**Objectives:** To evaluate the angiogenesis effect by the action of the monoclonal antibody Bevacizumab in the treatment of retrocervical endometriosis in Wistar rats.

**Design:** prospective and experimental study in Wistar rats

**Materials and Methods:** We studied 58 Wistar rats divided into three groups, Leuprolide, Bevacizumab and control respectively. The tissues were removed and fixed. The animals were divided into blades technique Tissue Micro Array, and prepared for immunohistochemistry. For staining was selected marker angiogenesis anti-VEGF.

**Results:** The mean reading by immunohistochemistry in Leuprolide group was 351.7  $\mu\text{m}^2$ , Avastin group was 73.8  $\mu\text{m}^2$  and 12.6  $\mu\text{m}^2$  in the Control group. The comparison between groups Avastin Lupron and Lupron and Control showed a reduction of endometrial implants in the group treated with Avastin ( $p < 0.001$ ). Between groups Avastin and Control ( $p = 0.171$ ).

**Conclusion:** The treatment of bevacizumab reduced endometrial implants but it was not effective in reducing angiogenesis in Wistar rats..

**Keywords:** Endometriosis, angiogenesis, bevacizumab

## Poster - Immunology and stem cells

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### EXPRESSION OF ADHESION MOLECULE CD166 IS REDUCED IN EUTOPIC ENDOMETRIUM, OVARIAN, AND COLO-RECTAL LESIONS OF WOMEN WITH ENDOMETRIOSIS

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**Objectives:** Endometrial stem cells may be involved in the pathogenesis of endometriosis. Our objective was to immunophenotype a subpopulation of stem-like cells found among stromal cells isolated from the eutopic and ectopic endometrium of women with ovarian and deep colorectal endometriosis, compared to cells isolated from healthy woman.

**Design:** Premenopausal women (n=15) were enrolled in a cross-sectional study. Women were not under hormonal therapy. Stromal cells from endometrial tissue were collected from women with (ESCE, n=6) and without (healthy, ESCC, n=5) endometriosis. Ovarian (OVAR, n=3) and colo-rectal (RECT, n=4) endometriotic stromal cells were also isolated.

**Materials and Methods:** After tissue digestion, stromal cells were isolated with appropriate sieves, expanded in Dulbecco's Modified Eagle Medium with 10% fetal calf serum. After 4 passages, cells were immunophenotyped using a FACS Aria flow cytometer and characterized by osteocyte and adipocyte differentiation. Bone marrow stem cells (BMSC, n=4) were used as positive controls.

**Results:** Flow cytometry analysis showed that ESCE, ESCC, OVAR, and RECT, were negative for hematopoietic (CD14, CD34, CD45, CD133, CD19), endothelial (CD106, CD31), and epithelial (EpCAM) markers. In contrast, >95% cells expressed markers of mesenchymal progenitors with no variation in mean fluorescence intensity (MFI) of CD73, CD29, and CD90 (P>0.05). However, CD105 MFI was significantly lower (P=0.005) in all cells when compared to BMSC, whereas CD166 MFI was significantly lower (P=0.01) in stromal cells from all sources of endometriosis patients (ESCE, OVAR, and RECT) when compared to BMSC and ESCC. The profile of surface markers indicates that stromal cells of all sources resemble BMSC, but are distinct from epithelial cells. The differentiation potential of all cells was comparable to BMSC, although adipocyte differentiation achieved unique features.

**Conclusion:** Stem cell surface markers and differentiation were similar between different sources of stromal cells. The reduction of CD166 expression in all tissues from endometriosis patients suggests a dysregulation of cell-to-cell interactions and may play a role in the pathogenesis of endometriosis. We thank the financial support of Ruhman Family.

**Keywords:** ALCAM, CD166, stroma

## Poster - Immunology and stem cells

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### INFERENCE OF AN ENDOMETRIOSIS-RELATED NETWORK OF INTERCELLULAR COMMUNICATION IN PERITONEAL FLUID SAMPLES

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**Objectives:** To improve the quantitative understanding of crosstalk between the immune response and soluble factors regulating the growth and breakdown of tissue during the development and progression of endometriosis.

**Design:** Retrospective analysis of an observational case-control study including 7 subjects with ASRM stage III or IV endometriosis and 6 control subjects undergoing surgery for other benign gynecologic conditions including pelvic pain, infertility, and leiomyoma.

**Materials and Methods:** Concentrations of 84 cytokines, proteases, growth factors, and shed receptors, many of which are known to be dysregulated in endometriosis, were measured using bead-based ELISAs in peritoneal fluid from subjects undergoing gynecologic surgery. Pearson correlations were calculated for all analyte pairs, and a network was constructed from the significant correlations.

**Results:** After multiple hypothesis correction, 3% (n=119) of the possible 3486 pair-wise correlations among the 84 analytes measured remained significant (p<0.05). The network coherently integrated numerous known direct interactions, including the effects of matrix metalloproteases (MMPs) 8 and 9 on IL-8; indirect interactions, such as the induction of MMP-9 by IL-1b; and relationships not previously been reported to play a role in the peritoneal environment, including positive correlations of MMP-12 with both RANTES and macrophage inhibitory factor (MIF). Importantly, 31 of the significant correlations were between proteases and cytokines or growth factors, suggesting substantial crosstalk between immune cells and endometriotic tissue. The most highly connected nodes included both cytokines and proteases, with IL-6, RANTES, TGF $\alpha$ , MMP-7, and bFGF each interacting with 12 or more partners.

**Conclusion:** As MMPs are known to regulate tissue breakdown prior to menstruation, the correlations found in this network analysis suggest a complex set of interactions between immune-mediated inflammation and the cycle of endometrial tissue growth and breakdown in endometriosis.

**Keywords:** Cytokine, protease, network

## Poster - Immunology and stem cells

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### ADVANCED OXIDATION PROTEIN PRODUCTS ARE INCREASED IN WOMEN WITH DEEP INFILTRATING ENDOMETRIOSIS

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**Objectives:** To evaluate oxidant (Advanced oxidation protein products (AOPP)) and antioxidant (Thiols) markers in sera and peritoneal fluid of women with various forms of endometriosis as compared to controls and investigate the correlation with disease activity.

**Design:** We conducted a laboratory study in a tertiary-care university hospital, between January 2011 and June 2013. This study enrolled a cohort of 245 patients: 137 with histologically proven endometriosis and 108 unaffected women. A thorough surgical examination of the abdominopelvic cavity was performed in all study participants.

**Materials and Methods:** For each patient blood samples and peritoneal fluids were obtained before and during surgical procedures, respectively. AOPP and Thiols levels were assayed in all study participants. The concentrations have been compared with the extent and the severity of endometriotic lesions according to the surgical classification.

**Results:** There was no difference in serum Thiols and AOPP levels between endometriotic and unaffected women. Peritoneal fluid Thiols levels were lower in endometriotic women as compared to controls without reaching statistical significance (median 128.08 pg/ml, range 106.32-149.61 pg/ml vs median, 137.08 pg/ml, range 121.14-153.03 pg/ml respectively; p=0.798). AOPP peritoneal fluids concentrations were higher in the endometriosis group (median, 204.59 pg/ml, range 92.45-357.01 pg/ml vs median, 177.94 pg/ml, range 130.68-225.21 pg/ml, respectively; p < 0.05). Instead, according to the surgical classification of endometriosis, we found that peritoneal AOPP levels were drastically increased in deeply infiltrating endometriosis (median, 278.53 pg/ml) as compared to endometriosis-free women (median, 177.94 pg/ml, p=0.001) or women affected by superficial endometriosis (median, 138.78 pg/ml, p=0.002) or endometrioma (median, 167.33 pg/ml; p=0.026).

**Conclusion:** Endometriotic women display significantly higher peritoneal AOPP levels than disease free controls, especially in case of deeply infiltrating endometriosis.

**Keywords:** Deep-infiltrating-endometriosis, thiols, advanced-oxidation-protein-products

Poster - Immunology and stem cells

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**MESENCHYMAL STEM CELLS TREATMENT IMPROVES THE ENDOMETRIOSIS PROLIFERATION IN CELL CULTURE.**

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**Objectives:** In order to improve the therapeutic potential of this gene therapy we combined it with cell therapy using human umbilical cord mesenchymal stem cells (hUCMSC).

**Design:** The levels of IL-1 $\beta$  were evaluated in the culture medium of normal and endometriotic endometrial cells transfected or not with Adp27EGFP and Adnull, and treated with hUCMSC.

**Materials and Methods:** Treatment with hUCMSC leads to increased IL-1 $\beta$  expression reaching endometriotic levels after 14 days of treatment even in the normal endometrial cells.

**Results:** Treatment with hUCMSC leads to increased IL-1 $\beta$  expression reaching endometriotic levels after 14 days of treatment even in the normal endometrial cells. The therapeutic effects of Adp27EGFP were totally inhibited in the endometriotic cells treated with hUCMSC. These results suggest that the mesenchymal stem cells can have a role in the progression of the endometriosis and cannot be used to treat the disease.

**Conclusion:** These results suggest that the mesenchymal stem cells can have a role in the progression of the endometriosis and cannot be used to treat the disease.

**Keywords:** Stem cells, p27

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### CHARACTERIZATION OF HUMAN ENDOMETRIAL STEM/PROGENITOR CELLS WITH AN ANIMAL MODEL OF ENDOMETRIOSIS

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**Objectives:** To identify progenitor stem cells in human endometrium transplanted into immunosuppressed mice using bromodeoxyuridine BrdU label retention and to characterize the microenvironment of these cells.

**Design:** Xenotransplantation of human eutopic endometrium hysterectomy tissue was performed under the kidney capsule of immunocompromised mice. Serial intraperitoneal injections of estradiol valerate and BrdU were applied, and the implants were analyzed by immunohistochemistry (IHC) and immunofluorescence (IF), to identify the presence of alleged stem cells and to characterize their niche.

**Materials and Methods:** A total of 21 mice were subjected to xenotransplantation and the grafts were collected between 8-12 weeks for IHC and IF assays with BrdU, estradiol receptor and progesterone receptor.

**Results:** We have identified alleged stem cells (BrdU positive cells) in xenoinplant human endometrium. They are located both in the stroma and in the glandular epithelium. Some of these cells present neither estrogen or progesterone receptors. Some of the BRDU positive cells (alleged stem cells) present only estrogen or progesterone receptors.

**Conclusion:** The human endometrium appears to exhibit stem cells both in the stroma and glandular epithelium. These cells might be responsible for the regenerative capacity of this tissue.

**Keywords:** Stem cells endometriosis

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### INCREASED EXPRESSION OF THE PLURIPOTENCY MARKER SOX2 AND NANOG IN OVARIAN ENDOMETRIOSIS

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**Objectives:** Endometriosis is chronic gynecological disorder and is classically defined as the presence of endometrial glands and stroma outside the uterine cavity. The precise etiology of endometriosis is not fully understood. This study aimed at analyzing the transcription pluripotency factor Sex-determining region Y-box 2 (SOX2), NANOG and octamer-binding protein 4 (OCT4) in the endometrium of women of reproductive age with and without ovarian endometriosis.

**Design:** a laboratory-based study

**Materials and Methods:** twenty-six women of reproductive age with laparoscopy-confirmed ovarian endometriosis and 16 women of reproductive age without ovarian endometriosis (control group) were recruited. Endometrial and endometriotic samples were collected and the expression of SOX2, NANOG and OCT4 were analyzed using quantitative real-time PCR, western blot and immunohistochemistry.

**Results:** Compared to control group, the eutopic endometrium of patients with ovarian endometriosis had higher mRNA and protein expression of SOX2, NANOG and OCT4, but only SOX2 showed significant difference. The mRNA and protein expression of SOX2 and NANOG increased significantly in the ectopic endometrium compared with the eutopic endometrium; while the ectopic endometrium had a trend towards lower OCT4 mRNA expression and higher OCT4 protein expression, which was not statistically significant.

**Conclusion:** The transcription pluripotency factor SOX2 and NANOG are increased in endometrial and endometriotic tissues of women of reproductive age with ovarian endometriosis. The over-expression of SOX2 and NANOG may contribute to the pathogenesis of endometriosis.

**Keywords:** Sex-determining region Y-box 2, NANOG, endometriosis

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### EXPRESSION OF ENDOGENEOUS RETROVIRUS GENE MRNA IN LOCAL ENDOMETRIOSIS

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**Objectives:** We reported the expressions of TLR7 and TLR9 mRNA in endometriosis. These mRNA activate immune cells through the recognition of endogenous DNA- or RNA-containing antigens. In SLE, the preferential production of these autoantibodies is apparently promoted by the presence of genetic abnormalities and induced expression of endogenous retroviruses.

**Design:** Experimental study We used endometriosis samples and endometrial tissues without endometriosis for control. We investigate the relationship between the expression of human endogenous retroviruses (HERV)-w, HERV-k mRNA and those of TLR7, TLR9, mPGES-1, and COX-2 mRNA.

**Materials and Methods:** Endometriosis samples were obtained from endometrial cyst. Endometrial tissues were obtained from the surgical specimen of benign gynecological conditions. Informed consents were obtained from all the patients in this study. The expression of HERV-w, HERV-k, TLR7, TLR9, mPGES-1, and COX-2 mRNA was examined by Quantitative real-time PCR.

**Results:** The expressions of HERV-w, HERV-k mRNA were detected in eutopic endometrium and endometriosis lesions. The expression levels of HERV-k mRNA in endometriosis samples were higher than those of eutopic endometrium of proliferative phase of endometriosis patients. In addition, the expression levels of HERV-k mRNA in peritoneal endometriosis were higher than those of eutopic endometrium of proliferative phase of endometriosis patients. There were relationships between expression levels of HERVs mRNA and those of COX-2 mRNA in endometriosis lesion.

**Conclusion:** The expressions of HERV-w, HERV-k mRNA of endometriosis samples indicate that autoimmune abnormality may play an important role in the pathogenesis of endometriosis.

**Keywords:** endometriosis HERV-w HERV-k

## Poster - Immunology and stem cells

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### EFFECT OF MISTLETOE ON ACTIVITY OF NK CELL IN ENDOMETRIOSIS

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**Objectives:** The purpose of this study is to investigate the cytotoxic effect and mechanism of NK cells in pelvic cavity fluids with endometriosis using mistletoe.

**Design:** in vitro experiments with Mistletoe and NK cells

**Materials and Methods:** Before and after mistletoe treatment, the cytotoxicity of NK cell was compared, and its effect for NK cell apoptosis was evaluated and the expression of CD107a directly participating in exocytosis of cytotoxic granules was compared.

**Results:** The cytotoxicity of NK cell showed significant difference between control group, endometriosis group A and group B, respectively 75.55%, 69.59% and 63.8%. The cytotoxicity of NK cell was significantly increased after treatment of mistletoe 200ng/ml. Before and after that in each group, respectively, it showed 81.64% vs 87.75% (P = 0.012) in control group, 78.30% vs 86.40% (P = 0.003) in endometriosis group A, and 73.67% vs 84.54% (P = 0.024) in endometriosis group B. The expression of CD107a was significantly increased after mistletoe treatment in each group. Before and after that, respectively, it showed 0.69% vs 1.51% (P = 0.012) in control group, 0.62% vs 1.19% (P = 0.003) in endometriosis group A, and 0.66% vs 1.50% (P = 0.024) in endometriosis group B.

**Conclusion:** Mistletoe directly influenced exocytosis of cytotoxic granules by increasing the expression of CD107a in NK cell, and consequently the cytotoxicity of NK cell was recovered normally. Therefore, it is expected that mistletoe is significantly effective material for the treatment of endometriosis.

**Keywords:** Endometriosis, NKcell, Mistletoe

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**EFFECT OF EXPERIMENTAL ENDOMETRIOSIS INDUCTION ON FOLLICLE DEVELOPMENT AND CORPUS LUTEUM REGRESSION IN A RAT MODEL**

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**Objectives:** Different mechanisms have been proposed to explain endometriosis associated infertility including alterations in follicular and peritoneal environment, in folliculogenesis and in granulosa cells function. The objective of this work was to evaluate the effect of endometriosis on follicle and corpus luteum development as well as apoptosis in the ovary.

**Design:** Two months old female Sprague Dawley rats were operated to either induce endometriosis or in a sham procedure. One month after surgery animals were sacrificed at proestrus. Ovaries were excised, one was fixed and the other one was frozen. Lesions were removed in order to histologically confirm endometriosis.

**Materials and Methods:** Follicles at different stages and corpora lutea were counted in ovary sections. Corpora lutea size was estimated measuring their diameter. Apoptosis was evaluated by Tunel in ovary slices. Pro- and anti- apoptotic proteins expression was assessed by western blot in total protein extracts from the ovary.

**Results:** The number of total ovarian structures was reduced in animals with endometriosis ( $p < 0.01$  versus sham). Females with endometriosis showed a reduced number of primordial, primary and preantral follicles ( $p < 0.05$ ) and a decrease in the percentage of primary follicles besides an increase in the percentage of atretic follicles ( $p < 0.05$ ). Corpora lutea diameter was decreased in rats with endometriosis ( $p < 0.05$ ). The percentage of late antral follicles that showed apoptotic cells was increased in the endometriosis group ( $p < 0.05$ ). The number of apoptotic cells per area of corpus luteum was increased in the endometriosis group ( $p < 0.01$ ). There were no changes in Bax and Bcl-2 expression between ovaries from endometriosis and sham rats, however the ratio Bcl-Xs/Bcl-Xl and the expression of procaspase-3 were significantly increased in the endometriosis group ( $p < 0.05$ ).

**Conclusion:** These results suggest that experimental endometriosis induction in rats causes a reduction in ovarian reserve and an increase in follicular atresia and luteolysis. These data support the hypothesis that abnormal folliculogenesis and impaired oocyte function would be implicated in endometriosis associated infertility. Bcl-Xs/Bcl-Xl would be involved in these processes.

**Keywords:** Infertility, apoptosis, folliculogenesis

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**PERITONEAL FLUID FROM INFERTILE WOMEN WITH MINIMAL/MILD ENDOMETRIOSIS MAY COMPROMISE THE SPINDLE OF METAPHASE II BOVINE OOCYTES**

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**Objectives:** Impaired oocyte quality may be involved in the etiopathogenesis of infertility-related endometriosis. Thus, this study aimed to evaluate the impact of peritoneal fluid (PF) of infertile women with and without minimal/mild endometriosis (EI/EII) on spindle integrity and chromosome alignment of bovine oocytes in vitro matured in the presence of PF.

**Design:** We performed an experimental study. From February 2009 to May 2010 PF samples were obtained from 12 women submitted to video laparoscopy (6 infertile women with EI/II and 6 fertile controls – FC), which were utilized in 6 in vitro maturation (IVM) experiments of immature bovine oocytes (IBO).

**Materials and Methods:** IBO were matured without PF (No-PF) and with three concentrations (1%, 5%, 10%) of two PF samples (EI/II and FC). The oocytes were fixed, stained for morphological visualization of both microtubules and chromatin, and analyzed by confocal microscopy. Data were analyzed by Poisson distribution, presented as mean percentage  $\pm$  SEM.

**Results:** The percentage of normal MII oocytes was significantly lower in the EI/II 1%, 5% and 10% concentrations ( $54.00 \pm 0.05$ ,  $30.42 \pm 0.07$ ,  $31.47 \pm 0.07$ , respectively) compared to the same concentrations in the FC group ( $73.21 \pm 0.05$ ,  $69.03 \pm 0.04$ ,  $67.07 \pm 0.04$ , respectively) and to the No-PF group ( $70.08 \pm 0.04$ ),  $p < 0.01$ . There were no differences between FC and No-PF groups. In the EI/II group, we observed significantly lower percentage of normal MII oocytes in the concentrations 5% ( $30.42 \pm 0.07$ ) and 10% ( $31.47 \pm 0.07$ ) compared to 1% ( $54.00 \pm 0.05$ ) demonstrating a concentration-dependent effect. In the FC group, no differences regarding the concentrations were found.

**Conclusion:** FP-EI/II promotes deleterious dose-dependent effect on spindle integrity and chromosome alignment of MII bovine oocytes in vitro matured. Thus this study opens a new perspective for understanding the pathogenesis of endometriosis-related infertility, suggesting that constituents of PF may be involved in the worsening of oocyte quality in women with EI/II.

**Keywords:** Endometriosis; peritoneal-fluid; oocyte-quality

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**L-CARNITINE PROTECTS AGAINST MEIOTIC DAMAGE INDUCED BY FOLLICULAR FLUID OF INFERTILE WOMEN WITH MILD ENDOMETRIOSIS USING A BOVINE MODEL**

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**Objectives:** The pathogenesis of endometriosis-related infertility has not been fully elucidated. This study aimed to investigate the potential protective effect of L-carnitine (LC) against deleterious substances present in the follicular fluid (FF) of patients with mild endometriosis (ME), which may affect the oocyte cytoskeleton and chromatin using a bovine model.

**Design:** We performed an experimental study. FF samples were obtained from 22 infertile women undergoing ovarian stimulation for intracytoplasmic sperm injection (11 with mild endometriosis -EFF- and 11 with tubal and/or male factor of infertility-CFF) which were pooled and utilized in 5 in vitro maturation (IVM) experiments with immature bovine oocytes (IBO).

**Materials and Methods:** IBO were submitted to IVM divided in five groups according to the addition of FF (1%) and LC (0,6mg/mL): without FF (NF), EFF, CFF, EFF + LC (ELC), CFF + LC (CLC). The oocytes were fixed, stained for morphological visualization of both microtubules and chromatin, and analyzed by confocal microscopy.

**Results:** Data were analyzed by Poisson distribution, presented as mean percentage  $\pm$  SEM. A total of 492 oocytes were visualized. No significant differences were found in the number of MII oocytes obtained in each group. The percentage of normal MII oocytes was similar comparing NF ( $87,24 \pm 0,05$ ) and CFF ( $77,33 \pm 0,05$ ) groups. The percentage of normal MII oocytes was significantly lower in the EFF group ( $51,44 \pm 0,06$ ) compared to NF and CFF groups. The addition of LC increased the percentage of normal MII oocytes in both ELC ( $74,12 \pm 0,05$ ) and CLC ( $91,17 \pm 0,05$ ) groups.

**Conclusion:** LC has a protective effect against meiotic damage induced by FF of infertile women with ME, suggesting that oxidative stress is involved in the worsening of oocyte quality. We question whether the use of LC as a supplement in patients with ME may be a novel approach to improve fecundity.

**Keywords:** Endometriosis; infertility; oxidative-stress

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**SYSTEMIC OXIDATIVE STRESS IN INFERTILE WOMEN WITH AND WITHOUT ENDOMETRIOSIS  
SUBMITTED TO OVARIAN STIMULATION**

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**Objectives:** Systemic oxidative stress(OS) might compromise oocyte quality and be involved in the etiopathogenesis of infertility related to endometriosis(E). Thus, the aim of this study was to compare eight OS markers in serum of infertile women with and without E submitted to controlled ovarian hyperstimulation(COH) for intracytoplasmic sperm injection(ICSI).

**Design:** A prospective controlled study was performed. Blood serum samples were obtained in early follicular phase of the menstrual cycle preceding COH (D1), after pituitary suppression (D2) and during COH (day of human chorionic gonadotropin (hCG) administration (D3) and day of oocyte retrieval (D4).

**Materials and Methods:** Serum from 118 women (61 with endometriosis and 57 control) was analyzed for total of hydroperoxydes(FOX1), glutathione(GSH), malondialdehyde(MDA) and advanced oxidation protein products(AOPP) by spectrophotometry; superoxide dismutase(SOD) and total antioxidant capacity(TAC) by immunoenzymatic assay; vitamin E(VIT E) by high performance liquid chromatography and 8-Hidroxi-2-deoxiguanosina(8OHdG) by ELISA. Statistical significance was 5%.

**Results:** GSH was significantly higher in serum of infertile women with endometriosis compared to control in D2 ( $p<0,01$ ), D3 ( $p<0,01$ ) and D4 ( $p=0,05$ ). FOX1 ( $p<0,01$ ) and SOD ( $p<0,01$ ) were significantly higher in women with E vs. control, respectively only in D4. 8OHdG was significantly lower in women with E vs. control in D1 ( $p<0,01$ ) and D3 ( $p=0,04$ ). TAC was significantly lower in women with E in all days analyzed ( $p<0,01$ ). No significant differences in the other OS markers were observed between groups.

**Conclusion:** Our data indicate the occurrence of systemic OS in infertile women with E submitted to COH. Lower levels in TAC may represent a higher consumption of enzymes by the antioxidant system in an attempt to prevent OS, resulting in DNA damage. Decreased levels of 8OHdG observed might corroborate this idea.

**Keywords:** Endometriosis, oxidative, serum

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### SERUM OXIDATIVE STRESS MARKERS AS PREDICTORS OF CLINICAL PREGNANCY IN INFERTILE WOMEN WITH MINIMAL/MILD AND WITH MODERATE/SEVERE ENDOMETRIOSIS AND WITHOUT ENDOMETRIOSIS SUBMITTED TO OVARIAN STIMULATION

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**Objectives:** Systemic oxidative stress(OS) related to endometriosis(E) might affect Assisted Reproduction Therapies(ART) results. Thus, the aim of this study was to analyze if specific OS markers in serum of infertile women with minimal/mild, moderate/severe E and controls submitted to controlled ovarian hyperstimulation(COH) could be used to predict ART outcomes.

**Design:** Prospective study. Serum samples of infertile women with minimal/mild, moderate/severe E and controls were obtained in early follicular phase of the menstrual cycle preceding COH. OS markers with accuracy higher than 70% were considered good predictors of clinical pregnancy and cut-off values favorable to gestational success after ART were determined.

**Materials and Methods:** Serum from 120 patients (36 minimal/mild E, 19 moderate/severe E and 65 control). Total of hydroperoxydes(FOX1), glutathione(GSH), malondialdehyde(MDA) and advanced oxidation protein products(AOPP) measurement by spectrophotometry; superoxide dismutase(SOD) and total antioxidant capacity(TAC) by immunoenzymatic assay; vitamin E(VIT E) by high performance liquid chromatography, 8-Hidroxi-2-deoxiguanosina(8OHdG) by ELISA. Statistical significance was 5%.

**Results:** MDA, AOPP and TAC showed to be good predictors of clinical pregnancy in infertile women with minimal/mild E and cut-off values were 22,23 µmol/g protein, 115,72 µmol/L, and 0,53 mEq Trolox®/L, respectively. MDA, 8OHdG, VIT E and SOD were good predictors in women with moderate/severe E and cut-off values were 15,70 µmol/g protein, 11,66 ng/mL, 25,12 µmol/L and 613,58 U/ml, respectively. FOX1, MDA, GSH and VIT E were good predictors in control group and cut-off values were 10,10 µmol/g protein, 15,89 µmol/g protein, 209,95 nmol/L and 18,05 nmol/L, respectively.

**Conclusion:** Our data indicate that serum OS markers present at the natural cycle previous to COH can be used as predictors of clinical pregnancy in infertile women with minimal/mild, moderate/severe and without E after ART. Cut-off values were determined, thus infertile women can be favored by antioxidant therapies in future approaches.

**Keywords:** Endometriosis, oxidative, pregnancy

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### OXIDATIVE STRESS MARKERS IN BLOOD SERUM FROM INFERTILE WOMEN WITH MINIMAL/MILD AND WITH MODERATE/SEVERE ENDOMETRIOSIS SUBMITTED TO OVARIAN STIMULATION

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**Objectives:** Infertility related to endometriosis(E) might be explained by systemic oxidative stress(OS), increased with the progression of the disease. Thus, the aim of this study was to compare eight OS markers in serum of infertile women with minimal/mild and moderate/severe E submitted to controlled ovarian hyperstimulation(COH) for intracytoplasmic sperm injection(ICSI).

**Design:** Prospective study. Blood serum samples of infertile women with minimal/mild and moderate/severe E were obtained in early follicular phase of the menstrual cycle preceding COH (D1), after pituitary suppression (D2) and during COH (day of human chorionic gonadotropin (hCG) administration (D3) and day of oocyte retrieval (D4).

**Materials and Methods:** Serum from 67 women (44 with minimal/mild and 23 moderate/severe E). Total of hydroperoxydes(FOX1), glutathione(GSH), malondialdehyde(MDA) and advanced oxidation protein products(AOPP) were measured by spectrophotometry; superoxide dismutase(SOD) and total antioxidant capacity(TAC) by immunoenzymatic assay; vitamin E(VIT E) by high performance liquid chromatography and 8-Hydroxi-2-deoxiguanosina(8OHdG) by ELISA. Statistical significance was 5%.

**Results:** GSH was significantly lower in serum of infertile women with moderate/severe E compared to minimal/mild E in D1 ( $p<0,01$ ). SOD was significantly higher in women with moderate/severe E vs minimal/mild E, in D4 ( $p<0,01$ ). TAC was significantly lower in women with moderate/severe E vs minimal/mild E in D4 ( $p<0,01$ ). No significant differences in the other OS markers were observed between groups.

**Conclusion:** Our data indicate the increase of systemic OS in infertile women with E submitted to COH as the disease progresses. Lower levels of GSH and TAC in serum of women with minimal/mild E may represent a higher consumption of enzymes by the antioxidant system in an attempt to prevent OS.

**Keywords:** Endometriosis, infertility, oxidative

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### EVALUATING THE IVF OUTCOME OF THE WOMEN WITH BILATERAL UNOPERATED ENDOMETRIOMAS

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**Objectives:** There is still some debate for the IVF outcome when bilateral endometriomas exist in the ovaries. So we aimed to evaluate the clinical pregnancy rate a retrospective manner in patients with bilateral unoperated endometriomas and compare them with controls.

**Design:** A retrospective cohort study in a single center

**Materials and Methods:** A retrospective comparative analysis was done about data from 108 patients with bilateral unoperated endometriomas and from 196 controls. Oocyte yield and quality, clinical pregnancies were compared during IVF treatment in women under 35 years of age done in Medicana International Istanbul Hospital, ART Center in Turkey.

**Results:** The ovarian response was significantly lower in women with bilateral endometriomas. The number of oocytes retrieved from case and from controls were  $6,1 \pm 3,3$  and  $8,9 \pm 4,5$  respectively ( $P < 0.05$ ). Oocyte retrieval was not hampered because of the endometriomas. The quality of oocytes were not different. Fertilization rates and the clinical pregnancy rates were not different either. (% 42,1 vs % 39,5)

**Conclusion:** The existence of endometriomas effects negatively the ovarian responsiveness but not the quality of oocytes and the pregnancy rates.

**Keywords:** bilateral endometrioma IVF

Poster - Infertility and ART

P-108

**FERTILITY BEFORE AND AFTER SURGERY FOR DEEP INFILTRATING ENDOMETRIOSIS WITH AND WITHOUT BOWEL INVOLVEMENT: A LITERATURE REVIEW**

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**Objectives:** The goal of this review was to assess the impact of various locations of deep infiltrating endometriosis (DIE) on spontaneous fertility and the benefit of surgery and Medically Assisted Reproduction (MAR) (in vitro fertilization and intrauterine insemination) on fertility outcomes.

**Design:** Systematic review of the literature.

**Materials and Methods:** MEDLINE search for articles on fertility in women with DIE published between 1990 and April 2013 using the following terms: “deep infiltrative endometriosis”, “colorectal”, “bowel”, “rectovaginal”, “uterosacral”, “vaginal”, “bladder” and “fertility” or “infertility”. Twenty-nine articles reporting fertility outcomes in 2730 women with DIE were analysed.

**Results:** Among the women with DIE and no bowel involvement (n=1295), no preoperative data on spontaneous pregnancy rate (PR) were available. The postoperative spontaneous PR rate in these women was 50.5% (95% Confidence Interval (CI) = 46.8-54.1) and overall PR (spontaneous pregnancies and after MAR) was 68.3% (95% CI = 64.9-71.7). No evaluation of fertility outcome according to locations of DIE was feasible. For women with DIE with bowel involvement without surgical management (n=115), PR after MAR was 29% (95% CI = 20.7-37.4). For those with bowel involvement who were surgically managed (n=1320), postoperative spontaneous PR was 28.6% (95% CI = 25-32,3) and overall postoperative PR was 46.9 % (95% CI = 42,9-50,9).

**Conclusion:** For women with deep infiltrative endometriosis without bowel involvement, surgery alone offers a high spontaneous pregnancy rate (PR). For those with bowel involvement, the low spontaneous and relatively high overall PR suggests the potential benefit of combining surgery and medically assisted reproduction.

**Keywords:** Endometriosis, deep, fertility

## Poster - Infertility and ART

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### ART WITH DIFFERED EMBRYO TRANSFER (ART-DET): A NEW OPTIONS IN ENDOMETRIOSIS (OSIS)

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**Objectives:** Endometriosis, a disease causing pain and infertility, is associated with functional alterations of the eutopic endometrium that hamper endometrial receptivity. The endometrium being normalized by ovarian blockage (GnRH-a and/or OCs), ART with differed ET (DET) while the ovaries are suppressed should be considered as viable option in case of endometriosis.

**Design:** Pilot study testing the ART-DET option in women having vulnerable embryos prior to offering this approach to women with endometriosis whose responses to COS is notoriously poor. For this, ART-DET was tested in women who had failed  $\geq 2$  prior ART cycles.

**Materials and Methods:** Women with  $\geq 2$  ART failures underwent COS using a GnRH antagonist with GnRH-a for final oocyte maturation. Embryos were vitrified using the following algorithm: If  $\leq 6$  zygotes were obtained, all were vitrified, but grown in culture and vitrified at the blastocyst stage if  $\geq 7$  zygotes were obtained.

**Results:** Data were analysed in 35 women, who fulfilled the protocol criteria. Results of the Per Protocol population were compared with those of: (i) 69 rank- and age-matched controls and (ii) 105 age-matched controls undergoing a 1st ART attempt. In 2/35(6%) cases no blastocysts were obtained and in 4 other, ETs were delayed for personal reasons. The 29 ET (9 of blastocysts 20 of day-2 embryos) gave rise to 12 ongoing pregnancies, for an oPR of 41.4 %/ET. These results were superior to findings made in rank- and age-matched controls – 65 ETs; oPR of 15.4%/ET ( $p < 0.006$ ). They are at par with those of age-matched controls undergoing a 1st ART attempt – 98 ETs; oPR of 29.6%/ET ( $p < 0.233$ ).

**Conclusion:** ART-DET was beneficial in women  $\geq 2$  prior ART failures whose ART chances are lower than same-age women undergoing a first ART attempt. This indicates that COS and ET can be dissociated even when pregnancy chances are suboptimal. Our data thus pave the way for using ART-DET in case of endometriosis.

**Keywords:** Differed transfer; endometrium

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### EXPERIMENTAL MODEL OF ENDOMETRIOSIS AND INFERTILITY IN AN ANIMAL MODEL

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**Objectives:** To develop an experimental model of peritoneal and retrocervical endometriosis in rabbits and fertility's findings

**Design:** Prospective study comparing peritoneal and retrocervical endometriosis in animal model

**Materials and Methods:** 30 female rabbits were divided into three groups: Control (n = 10) Retrocervical (n = 10) and Peritoneal (n = 10) and 21 days after surgery the rabbits were put to copulate. Then, pregnancy and abortion, was evaluated by ultrasonography. After the animals were euthanized, microscopic analysis were performed.

**Results:** Study of experimental induction of endometriosis – Retrocervical Group: 70% of implants in activity, 60% with adhesion and 40% with cyst. Peritoneal Group: 100% of implants in activity, 20% with adhesion and 50% with cyst. Study of fertility - Control Group: 77.8% fertility (22.2% abortion, 33.3% fetal death and 22.2% of term births). Retrocervical Group: 80% fertility (20% fetal death and 60% of births at term). Peritoneal Group: 70% fertility, all full-term births

**Conclusion:** There was no difference in fertility between peritoneal and retrocervical groups. The experimental model of retrocervical endometriosis in rabbits is reproducible and might be useful for new treatments

**Keywords:** Endometriosis,infertility, rabbits

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**ENDOMETRIOSIS RELATED INFERTILITY: PAINFUL SYMPTOMS ARE ASSOCIATED WITH DEEP INFILTRATING ENDOMETRIOSIS**

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**Objectives:** To evaluate the significance of severe painful symptoms for endometriotic women presenting with infertility.

**Design:** We conducted a cross sectional study in a tertiary-care university hospital between January 2004 and March 2013. This study enrolled a cohort of 870 patients with histologically proven endometriosis who underwent surgery for pain and/or infertility. Complete surgical excision of all recognizable endometriotic lesions was achieved in each patient.

**Materials and Methods:** For each patient data were collected preoperatively using a structured questionnaire. The pain was considered severe when the VAS  $\geq 7$ . Infertile endometriotic women were compared according to the existence of severe pain or not. Disease severity was evaluated using both rAFS and surgical classifications.

**Results:** In the whole endometriotic population women with infertility were more likely to have a previous history of surgery for endometriosis (PHSE) than women without infertility (137/307 (44.6%) vs 195/562 (34.7%);  $p=0.004$ ). In addition women with infertility showed a more aggressive disease with higher rAFS adhesion scores ( $24.2 \pm 26.2$  vs  $18.1 \pm 22.8$ ;  $p=0.001$ ) and more severe deep infiltrating endometriosis (DIE) multifocal and with intestinal involvement ( $p=0.009$ ). Among endometriotic women with infertility, severe painful symptoms ( $n=223$ ) were associated with PHSE (14/84 (16.7%) vs 123/223 (55.2%);  $p<0.001$ ) as compared to women with moderate or no painful symptoms ( $n=84$ ). In addition women with infertility and severe pain showed a more aggressive disease with higher rAFS adhesion scores ( $29.2 \pm 26.8$  vs  $10.9 \pm 19.2$ ,  $p<0.001$ ) and associated DIE (153/223 (68.6%) vs 19/84 (22.6%),  $p<0.001$ ).

**Conclusion:** In case of infertility, severe pelvic pain is significantly associated with previous history of surgery for endometriosis, higher rAFS adhesions scores and associated deeply infiltrating lesions. In this situation, the practitioner should address the patient to a referral centre.

**Keywords:** Infertility, endometriosis, pain

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### EFFICACY OF INTRAUTERINE INSEMINATION IN MODERATE TO SEVERE ENDOMETRIOSIS. A SYSTEMATIC REVIEW AND META-ANALYSIS OF OBSERVATIONAL DATA.

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**Objectives:** A systematic review and meta-analysis is conducted to evaluate the efficacy of intrauterine insemination (IUI), since the role of this treatment strategy in moderate to severe endometriosis patients suffering from subfertility is discussed in literature.

**Design:** To identify all relevant publications systematic searches were performed in the bibliographic databases PubMed, EMBASE, Cinhal and The Cochrane Library from inception to September 12th, 2013. Search terms expressing 'endometriosis' were used in combination with terms comprising 'IUI'. Two reviewers independently screened all potentially relevant titles and abstracts for eligibility.

**Materials and Methods:** Studies including moderate to severe endometriosis patients reporting pregnancy rates after IUI were selected. Studies were excluded if pregnancy was not specified for moderate to severe endometriosis patients receiving IUI treatment. A weighed mean pregnancy rate per patient and cycle was calculated by using Microsoft Excel (Neyeloff et al. 2012).

**Results:** Our search revealed 510 unique citations. Seventeen articles fulfilled our criteria; after exclusion of one article due to overlapping data and inclusion of our own data (article submitted), seventeen articles (12 retrospective; 5 prospective) were included for the analysis. Pregnancy was defined as biochemical in four, clinical in ten, ongoing in one and not further defined in two articles. Seven studies included patients/cycles pretreated with GnRH analogues (two weeks – six months). Fourteen studies reported pregnancy per patient; 165 pregnancies in 474 patients (34.8%). Thirteen studies reported pregnancy per cycle; 140 pregnancies in 1088 cycles (12.9%). The calculated weighed mean pregnancy rate per patient was 32.3% (95%CI 22.7%-41.9%); the calculated weighed mean pregnancy rate per cycle was 12.4% (95%CI 8.1%-16.7%).

**Conclusion:** This meta-analysis of observational data showed that IUI could be a valuable treatment in moderate to severe endometriosis. Whether this treatment can be structurally offered prior to IVF must be investigated in a randomized controlled trial including efficacy, safety and cost-effectiveness.

**Keywords:** Meta-analysis, IUI, pregnancy

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**RESULTS OF ICSI-IVF IN WOMEN AFTER COLORECTAL RESECTION FOR DEEP INFILTRATIVE ENDOMETRIOSIS: RESULTS OF A PRELIMINARY STUDY**

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**Objectives:** To evaluate fertility in women after colorectal resection for deep infiltrating endometriosis (DIE). We evaluated fertility after ICSI-IVF cycles.

**Design:** We present preliminary results of a prospective cohort study including all women who had a complete resection of DIE with a colorectal resection and had at least one ICSI-IVF cycle in our center from January 2005 to June 2013.

**Materials and Methods:** At the time of this abstract, 33 of 50 women with 1 to 4 ICSI-IVF cycles were included. We evaluated pregnancy rate and cumulative pregnancy rate (CPR). CPR was calculated using cumulative-incidence methods from log-rank test and Kaplan-Meier curves. Univariate analysis was used to identify determinant factors of CPR.

**Results:** The median number of ICSI-IVF cycles was 1 (range 1-4). Median age at the beginning of the first ICSI-IVF procedure was 32 years (range 26-38) and median duration between surgery and this procedure was 17 months (range 7-120). Twenty-three women (69.7%) became pregnant after ICSI-IVF cycles. The CPR after four ICSI-IVF cycles was 86.4%. We found no impact of associated adenomyosis, women age over 35 years and anti-Mullerian hormone serum level under 2ng/ml on CPR. Five women (15%) had ICSI-IVF cycles before surgery with no pregnancy. Of these, three (60%) became pregnant after surgery. Two became pregnant after one ICSI-IVF cycle and one after three cycles.

**Conclusion:** Theses preliminary results show high CPR after ICSI-IVF in women who previously underwent colorectal resection for DIE. Moreover, additional pregnancies were obtained in women with previous failure of ICSI-IVF cycles before surgery.

**Keywords:** colorectal endometriosis, ICSI-IVF

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**ULTRALONG PROTOCOL AND ETHANOL SCLEROTHERAPY BEFORE IVF FOR RECURRENT ENDOMETRIOMAS AND LOW OVARIAN RESERVE**

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**Objectives:** to analyse the IVF results among patients with recurrent endometriomas and low ovarian reserve after a combined preparation including GnRH analogues and ethanol sclerotherapy

**Design:** Prospective analyse of a procedure to take in charge recurrent endometriomas before ART

**Materials and Methods:** 31 cycles among 21 patients received a 3 month GnRH analogues regimen. After one month, an ethanol sclerotherapy was done under ultrasound control. 45 days latter IVF ovarian stimulation with HMG was started. Ovum pickup was done even if only one follicle was growing.

**Results:** one cycle was cancelled for absence of ovarian response. The means number of recovered oocytes was 6.2 and the median was 4. The means number of obtained embryos was 3.7 and the median was 3. 27 transfers were done (90%) with a mean number of transferred embryo of 1.33. 11 implantations occurred resulting in 3 miscarriages , one ectopic pregnancy and 8 deliveries or still ongoing pregnancies (25.8 % per started cycles). One ovarian abscesses occurred

**Conclusion:** : despite a short series, this result appears encouraging (25.8 % deliveries per started cycles) among prognosis patients. This method is an excellent alternative to iterative surgery. It should be more largely evaluated in a multicentre prospective study

**Keywords:** ART, sclerotherapy, endometriomas

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### ENDOMETRIOSIS FERTILITY INDEX (EFI) AS A PREDICTOR OF PREGNANCY AFTER LAPAROSCOPIC SURGERY IN ENDOMETRIOSIS-ASSOCIATED INFERTILITY

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**Objectives:** To evaluate the value of endometriosis fertility index (EFI) in the prediction of pregnancies after laparoscopic surgery for endometriosis in the absence of assisted reproduction technology (ART) treatments.

**Design:** Retrospective (May 2008 - October 2010) and prospective (November 2010 – January 2013) study where the EFI was calculated based on historical and surgical factors prospectively registered. Only clinical pregnancies in women attempting non-ART conception after laparoscopic endometriosis surgery were considered.

**Materials and Methods:** From May 2008 to January 2013, 150 patients underwent laparoscopic surgery for infertility associated endometriosis. Exclusion criteria: lost for follow-up, ovarian suppression medication for pain or severe male factor. As in our public unit there is a 12 months waiting list, all included participants attempted non-ART conception immediately after surgery.

**Results:** Out of the 150 patients diagnosed with endometriosis 33 fulfilled the exclusion criteria. EFI was calculated for the remaining 117. Pregnancy was achieved in 36 through non-ART methods. From the 36 women, 23 achieved pregnancy spontaneously, 12 after intra-uterine insemination and 1 after ovulation-induction. Within 12 months after surgery, the cumulative overall pregnancy rate was 27.3% [95% confidence interval (CI) 20.2-36.4], ranging from 14.3% [95% confidence interval (CI) 2.1-66.6] for EFI score 4, to 66.7% [95% confidence interval (CI) 22.5-99] for EFI score 10. No pregnancy occurred in the small group with EFI<4 (6 patients). After 12 months the results are meaningless because patients are then included in the ART program.

**Conclusion:** In spite of a lower overall pregnancy rate (probably resulting from decisions to operate cases of endometriosis usually directly included in ART, imposed by long waiting list), in our reality EFI still seems a useful tool to be used in guiding post-surgical management and counseling.

**Keywords:** endometriosis, pregnancy, EFI

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### RECURRENT ENDOMETRIOMA:A NEW PROTOCOL PRECEDING ART

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**Objectives:** To evaluate the effectiveness of a new protocol preceding ovarian stimulation for IVF in women with endometrioma measuring 4 cm or more.

**Design:** It is a retrospective study of women < 37 years age, having diagnosed with an endometrioma of 4 cm or more undergoing their first cycle of ovarian stimulation for IVF. Women with more than one previous unilateral cystectomy or those with bilateral cystectomy were excluded.

**Materials and Methods:** The selected patients were given long GnRH depot 11.25/22.5 mg for pituitary/ovarian suppression. After a period of 2 months, the cyst was aspirated trans-vaginally and diluted tetracycline was injected for sclerotherapy. From day 2 of the spontaneous cycle, we started the ovarian stimulation.

**Results:** Out of the performed 256 cases till date, the results may be noted as follows : At the end of suppression the size reduction in the cyst was noted in the range of 50 % to 75 % from the original size . Mean Gonadotrophin dose was 3357 IU, Mean oocytes retrieved were 6.2%, Fertilization rate was 73% and Day 3 top quality embryos were 52.7 % It also resulted in a Clinical pregnancy rate of 32.6 % and implantation rate of 18.6% .

**Conclusion:** The 3 step protocol has the potential to maximize the chance of success and minimize the risk in the difficult treatment of this patient group with poor ovarian reserve. Further larger studies in this regard are needed to confirm the findings of our analysis.

**Keywords:** Recurrent endometrioma, ART, Long agonist

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**SECOND PREGNANCY IN OPERATED INFERTILE ENDOMETRIOTIC PATIENTS WITH A FIRST BABY OBTAINED BY IN VITRO FERTILIZATION: AN OBSERVATIONAL STUDY.**

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**Objectives:** to determine prognostic factors for a second pregnancy after a first pregnancy obtained by Assisted Reproductive Technologies (ART).

**Design:** Observational study from January 2004 to December 2012 in a French University ART center

**Materials and Methods:** 65 initially operated infertile and endometriotic patients desired a second pregnancy after a first pregnancy obtained by ART. Spontaneous pregnancy, ART pregnancy, and cumulated (spontaneous & ART) pregnancy rates were calculated. Other good prognostic factors for spontaneous pregnancy were explored

**Results:** no patient was operated on a second time. In all, 78% of patients conceived (50 pregnancies). No difference was found between spontaneous pregnancy (54%) and ART pregnancy (46%). Age, endometriosis staging, least function score, complete removal of endometriotic lesions and pelvic adhesions were not different. The median spontaneous conception time was 17 months after the first delivery

**Conclusion:** pregnancy rates for a second pregnancy in initially infertile endometriotic patients were high, and 54% of pregnancies were obtained spontaneously. Our results should be confirmed with large prospective studies

**Keywords:** EFI, surgery, Pregnancy

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**ROLE OF LAPAROSCOPIC SEGMENTAL BOWEL RESECTION FOR ENDOMETRIOSIS IN PATIENTS WITH FAILED IN VITRO FERTILIZATION CYCLES**

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**Objectives:** The aim of this study was to describe our results related to fertility, pregnancy outcomes and their determinant factors in patients with previous IVF failures who conceived after laparoscopic segmental bowel resection due to endometriosis.

**Design:** We have designed a prospective study.

**Materials and Methods:** Were evaluated from January 2009 to September 2013, 145 women that had undergone ICSI treatments. All women underwent transvaginal sonography with bowel preparation, to evaluate size and wall infiltration of lesions in retosigmoid, and all of them were submitted to a segmental colorectal resection.

**Results:** 145 women with prior IVF or ICSI failures were evaluated. The medium age was 34 years (range 32-39). Between them, 106 (73%) conceived after laparoscopic resectosigmoidectomy due to endometriosis, including 65 (61,3%) spontaneous pregnancies and 41 (23,5%) using ICSI technology (in less than three consecutive cycles). Mean follow-up after segmental colorectal resection was two years (range: 6–56 months). The median time to conceive after surgery was 8 months. Besides the high pregnancy rate, all patients have had positive effects on endometriosis-related symptoms as dysmenorrhea, pelvic pain not related to menstruation, dyspareunia, besides bowel symptoms as pain, diarrhea or constipation.

**Conclusion:** Laparoscopic segmental bowel resection in cases of deep endometriosis may be considered for the treatment of endometriosis even after multiple IVF failures.

**Keywords:** IVF failure, endometriosis

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**ENDOMETRIOSIS IS NOT ASSOCIATED WITH A REDUCED RISK FOR TWIN PREGNANCIES AFTER TRANSFER OF TWO EMBRYOS IN AN ART CYCLE**

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**Objectives:** A reduced chance to achieve pregnancy has been described for women with endometriosis. There is still a debate on reducing number of transferred embryos to reduce the risk for multiple pregnancies. Is there a reduced risk for women with endometriosis to achieve a twin pregnancy after a two embryo transfer?

**Design:** Retrospective Study in an ART collective.

**Materials and Methods:** In this study 3390 women with a two embryo transfer in an ART trial according to different characteristics including diagnosis of sterility were analysed.

**Results:** Endometriosis as diagnosis was found in 393 women (11.6%). The adjusted odds ratio of a twin pregnancy in women with endometriosis was 1.103 (95% CI 0.761 - 1.599). Women with endometriosis are not at a reduced risk to achieve a twin pregnancy after transferring two embryos in an ART trial.

**Conclusion:** As there is no reduced risk for twin pregnancy in women with endometriosis after transfer of two embryos in an ART trial the number of embryos to transfer should be reconsidered according to twin pregnancy associated risks.

**Keywords:** ART, endometriosis, twin-pregnancy

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### EFFICACY AND SAFETY OF INTRAUTERINE INSEMINATION IN PATIENTS WITH MODERATE TO SEVERE ENDOMETRIOSIS

Lisette Van Der Houwen<sup>1</sup>, Anneke Schreurs<sup>1</sup>, Roel Schats<sup>1</sup>, Cornelis Lambalk<sup>1</sup>, Peter Hompes<sup>1</sup>, Velja Mijatovic<sup>1</sup>

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**Objectives:** This study was performed to evaluate the efficacy and safety of two different IUI treatment strategies and the additional effect of long term pituitary down-regulation in moderate to severe endometriosis patients.

**Design:** A retrospective analysis was established including all patients with surgically confirmed moderate to severe endometriosis patients (stage III - IV), who started their IUI treatment between January 2007 and July 2012. Up to a maximum of six cycles were included.

**Materials and Methods:** Two treatment strategies were compared; IUI with controlled ovarian hyperstimulation (COH) (n = 20, 61 cycles, IUI+COH) versus IUI without COH in the first three cycles followed by IUI with COH (n = 45, 184 cycles, IUI+natural/COH). Also, the additional effect of preceding long term pituitary down-regulation was investigated.

**Results:** Eight (40.0%) and 7 (15.6%) ongoing pregnancies were accomplished in patients undergoing IUI+COH and IUI+natural/COH, respectively (p=0.05). Cox regression analysis showed a HR of 3.2 (95%CI 1.1-8.5, p=0.02), reflecting a significantly higher chance on ongoing pregnancy in patients receiving IUI+COH. Preceding long term pituitary down-regulation tended to result in a higher ongoing pregnancy rate (adjusted HR 1.8, 95%CI 0.6-5.1, p=0.26). Eight (40.0%) versus 16 (35.6%) recurrences of endometriosis complaints were reported in patients undergoing IUI+COH versus IUI+natural/COH, respectively (p=0.73). Preceding long term pituitary down-regulation tended to result in a higher chance on endometriosis recurrence (adjusted HR 2.3, 95%CI 0.98-5.3, p=0.06).

**Conclusion:** IUI with COH could be a valuable treatment in moderate to severe endometriosis patients. Preceding long term pituitary down-regulation might positively influence the ongoing pregnancy rate and can be considered. Whether this treatment strategy can be structurally offered prior to IVF must be investigated in a randomized controlled trial.

**Keywords:** IUI, ongoing pregnancy, recurrence

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### DOES THE PRESENCE OF ENDOMETRIOSIS IMPAIR IN VITRO FERTILIZATION (IVF) RESULTS?

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**Objectives:** Evaluate whether the presence of endometriosis compared to tubal factor infertility impairs the efficacy of in vitro fertilization in terms of response to controlled ovarian hyperstimulation (COH), fertilization and pregnancy rates

**Design:** Retrospective observational study of 344 consecutive IVF cycles performed from January 2011 to July 2013 at Pró-Criar Reproductive Medicine Center.

**Materials and Methods:** Two groups were formed: tubal factor (n=182) and endometriosis (n=162). Outcomes evaluated were female age and weight, basal FSH, number of hMG ampoules used, length of COH, number of mature oocytes collected and fertilized, cleavage rate, number of embryos transferred and cryopreserved and pregnancy rates.  $p < 0.05$  was statistically significant.

**Results:** Female age was the only outcome reaching significance ( $p=0,024$ ). The other clinical and laboratory outcomes evaluated did not show any significant differences between groups: weight ( $p=0,558$ ), basal FSH ( $p=0,842$ ) and estradiol ( $p=0,457$ ) levels, initial number of hMG ampoules used ( $p=0,115$ ), total number of hMG ampoules used ( $p=0,533$ ), length of COH ( $p=0,374$ ), number of mature oocytes collected ( $p=0,368$ ) and fertilized ( $p=0,132$ ), number of cleaving oocytes ( $p=0,122$ ), number of embryos transferred ( $p=0,092$ ) and cryopreserved ( $p=0,083$ ) as well as pregnancy rate ( $p=0,093$ ).

**Conclusion:** Patients with endometriosis-associated infertility undergoing IVF respond as well as women with tubal-factor infertility in terms of number of mature oocytes, fertilization and pregnancy rates and number of embryos available for cryopreservation.

**Keywords:** ART, endometriosis, pregnancy

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### THE ENDOMETRIOSIS FERTILITY INDEX (EFI): REVIEW OF 4 STUDIES VALIDATING THE EFI AND NOVEL EFI-BASED TREATMENT RECOMMENDATIONS FOR GYNECOLOGISTS GLOBALLY

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**Objectives:** To review studies that assessed the validity of the EFI in different populations and recommend novel treatment algorithms based on further analysis of the EFI.

**Design:** Literature review and additional retrospective analysis of data from the original EFI.

**Materials and Methods:** Review of PubMed and the Internet for research studies that evaluated EFI use in populations different than those in which the EFI was initially derived. Published data used to create the EFI were then used to create tables and algorithms to aid clinicians in the practical application of the EFI.

**Results:** 4 studies have evaluated the EFI. The first (n=233) found the relationship between the EFI and non-ART pregnancy to be highly significant. The second (n=350) confirmed the EFI is meaningful to guide post-surgical treatment. The third (n=132) concluded the EFI is a simple and reliable tool to predict pregnancy in patients with surgically-documented endometriosis followed by IUI or IVF management. The fourth (n=199) concluded the EFI provides an important reference to predict post-operative pregnancy. EFI score, age-weighted, endometriosis treatment algorithms for the first, second and third year after treatment include four possible recommendations: attempt non-ART conception for at least one year; probable attempt non-ART conception, consider role of IVF; probable IVF, refer to specialist for management, and; refer for IVF.

**Conclusion:** The EFI is the only endometriosis staging/classification system that has been validated internally to predict pregnancy rates. The simple, robust EFI has been further validated in 4 different populations in Belgium, France and China. Detailed clinical treatment recommendations based on the EFI can now be used by gynecologists globally.

**Keywords:** Endometriosis, fertility, index

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### FERTILITY OUTCOME AFTER SEGMENTAL BOWEL RESECTION FOR ENDOMETRIOSIS

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**Objectives:** To report the effect of laparoscopic segmental bowel resection over the reproductive outcome in women with bowel endometriosis

**Design:** Retrospective study. Intervention: Laparoscopic excision of DIE of the pelvis, with segmental bowel resection and primary anastomosis.

**Materials and Methods:** Main Outcome Measure(s): Fertility outcome, either spontaneous and after in vitro fertilization. Secondary Outcome Measure(s): Dysmenorrhoea, dyspareunia, non-menstrual cyclic pain and dyschesia improvement.

**Results:** Mean follow-up was 33.5 months and mean age of patients was 31 year-old. Global pregnancy rate was 57.6% (15/26), and in infertile women wishing to conceive, cumulative pregnancy rate was 72% (13/18). In this later group, 77% (10/13) of the pregnancies were conceived spontaneously and 23.1% (3/13) after subsequent in vitro fertilization. Women younger than 35 year-old presented a higher spontaneous pregnancy (66.7%) in comparison to 33% in women aged 35 or more.

**Conclusion:** Laparoscopic excision of deep infiltrating endometriosis with segmental bowel resection may enhance fertility, increasing significantly the rate of spontaneous conception especially in women younger than 35 years old.

**Keywords:** Bowel resection infertility

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### EXISTANCE OF LARGE ENDOMETRIOMAS DOES NOT MAKE A DIFFERENCE IN PREGNANCY RATES BETWEEN FRESH AND FROZEN BLASTOCYST TRANSFERS IN ART

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**Objectives:** To investigate if there is a difference of the pregnancy rates between fresh and vitrified blastocyst transfers in women with large endometriomas

**Design:** We performed a retrospective, database-searched cohort study.

**Materials and Methods:** A retrospective comparative analysis was done in IVF Center, Medicana International Istanbul Hospital, Turkey. Sixtyseven fresh blastocyst transfer cycles and 39 frozen-thawed single blastocyst transfer cycles in women with endometrimas larger than 4 cm were compared. All women were under 39 years of age.

**Results:** Of the 67 cycles in the fresh transfer group, there were 29 clinical pregnancies and the clinical pregnancy rate was 43,2 %. There were 17 pregnancies of the 45 cycles in the vitrified-thawed group, and the clinical pregnancy rate was 37,7 %. The implantation rate and ongoing pregnancy rate did not differ significantly between the two groups. Also the miscarriage rate was the same.

**Conclusion:** The existance of large endometriomas should not effect the decision for making the transfer in fresh or frozen-thawed cycle. Surgery may be deferred after the ART treatment and the probable pregnancy.

**Keywords:** endometrioma, IVF, vitrification

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### FERTILITY OUTCOME AFTER LAPAROSCOPIC SEGMENTAL BOWEL RESECTION FOR ENDOMETRIOSIS

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**Objectives:** The aim of the present prospective study was to investigate fertility, pregnancy rate and outcomes in women who underwent recto sigmoid resection because of symptomatic bowel endometriosis.

**Design:** We have designed a prospective study.

**Materials and Methods:** Between July 2009 and July 2013, we have evaluated prospectively 350 women who underwent segmental bowel resection for endometriosis. 322 women had bowel symptoms as pain during evacuation, diarrhea, constipation, abdominal bloating, and/or dyschezia. Besides, 196 women (56%) had an associated infertility. All patients were submitted to laparoscopic procedure.

**Results:** Between infertile patients, the mean duration of infertility before surgery was 18 months (range, 12–32 months). Of these infertile women, 74% (145 women) underwent some infertility treatment (IUI or IVF) before surgery. Patients mean age was 33.6 years (range: 24–41). Thirty six women (18%) had an associated male infertility. One hundred and forty one women (72%) had at least one previous surgery for endometriosis. After surgical procedure, 133 (68%) pregnancies were obtained, including 98 spontaneous (73,7%) and 35 by IVF (26,3%). The mean time to conceive was 8 months. Nine patients have had spontaneous miscarriages.

**Conclusion:** In conclusion, our results support that segmental laparoscopic bowel resection for endometriosis in symptomatic women with associated infertility is feasible effective and safe and offers high pregnancy rates.

**Keywords:** Fertility, bowel endometriosis

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### ART, ENDOMETRIOMAS (OMA) AND PELVIC INFECTIONS: AN UNEXPECTED CLINICAL PICTURE.

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**Objectives:** OMAs should not be removed before ART, as it likely hampers outcome. ART with OMA however increases the risk of infectious complication. As we feared that such infectious complications were under-reported, we retrospectively analyzed 4 years of our own ART activity and records of emergency admissions in women with endometriosis.

**Design:** Retrospective cohort analysis over 4 consecutive years based on medical records and coding system in a university-base endometriosis and ART reference center.

**Materials and Methods:** We retrieved all the patient charts identified as emergency admission for 'infectious' processes w/-or-w/o 'peritonitis', w/-or-w/o 'TOA' in women also diagnosed 'endometriosis' in 2009-2012. The targeted charts were individually analyzed for categorization of the infectious episode and determining whether ART had been performed.

**Results:** Of the 230 identified patients, 213 actually had a scheduled surgery misclassified as an emergency pelvic infection and were thus excluded. Five patients who had surgery for endometriosis <1 month earlier and 1 patient with insufficient data were also excluded. All the 11 patients retained for analysis had an emergency admission with fever, acute abdominal and elevated WBC count (>13.109/l). An adnexal mass was found on ultrasounds in all. Of the 11 infectious processes, 3 were in women who had ART-with-OMA 16, 57 and 102 days earlier. In the remaining 8 cases a TOA occurred spontaneously in women who never had ART. The TOA was associated with an existing OMA in 5 women, while the remaining 3 had no OMA.

**Conclusion:** We unveiled the unforeseen possibility that some complications of ART and OMA are not linked to ART, but rather constitute a sporadic occurrence in endometriosis. Finding that all infectious complications seen after ART are not necessarily linked to ART further supports our recommendation of not removing OMAs before ART.

**Keywords:** ART, endometrioma, infection

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**NONSURGICAL TRANSVAGINAL SONOGRAPHY GUIDED ASPIRATION/SCLEROSIS (TVS-A/S) OF OVARIAN ENDOMETRIOMATA (OE) PRIOR TO LUTEAL PHASE GNRHA/CONTROLLED OVARIAN HYPERSTIMULATION (COH) FOR IVF-ET.**

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**Objectives:** To evaluate the safety and efficacy of TVS-A/S for large or multiple OE prior to IVF-ET and the effect on COH, egg quality and pregnancy outcome, while avoiding the risks and cost of additional surgeries for severe endometriosis.

**Design:** Ongoing prospective observational clinical study.

**Materials and Methods:** Patients with recurrent OE following 1-4 (mean 2.38) surgeries for Stage IV endometriosis from 2/05-6/13 were studied. TVS-A/S using a 14g needle was performed under conscious sedation. Erythromycin 500 mg. in D5W containing 1% lidocaine was used for sclerosis. OE size, number, tolerability, side effects, COH and IVF-ET were compared.

**Results:** 46 patients, age 24-44 (mean 36.3 yrs.) with 1-4 (mean 2.3) OE measuring 13-68 mm. (mean 38 mm.) underwent TVS-A/S. 41 patients underwent COH for IVF-ET using luteal phase GnRHa and HMG. 59.8% of patients had endometriosis noted at follicular aspiration, with OE of 10-26 mm. for an average reduction size of OE of 32.6 mm. ( $p < .001$ ). 3-18 (mean 7.46) oocytes were retrieved with a fertilization rate of 63.6% (range 0%-100%). 40/41 cases resulted in ET of 2-4 (mean 3.2) embryos with a clinical pregnancy rate of 52.5%. 21 cases yielded embryos for cryopreservation. There were no major complications.

**Conclusion:** Nonsurgical TVS-A/S of OE appears to be safe and effective in reducing OE volume prior to IVF-ET and may maintain pregnancy rates in poor prognosis patients while avoiding the risks of further surgical intervention.

**Keywords:** endometrioma, IVF

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**THE SIDE OF OVARIAN ENDOMETRIOMA DOES NOT AFFECT THE OUTCOME OF IVF/ICSI IN INFERTILE WOMEN UNDERGONE LAPAROSCOPIC CYSTECTOMY**

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**Objectives:** To assess the impact of the laterality of ovarian endometrioma on pregnancy outcome of in vitro fertilization/intracytoplasmic sperm injection (IVF/ICSI) in infertile patients undergoing laparoscopic cystectomy.

**Design:** A retrospective cohort study of 103 IVF/ICSI cycle in patients who previous underwent laparoscopic cystectomy for unilateral endometriomas using an electronic database and patients' files.

**Materials and Methods:** There were 41 cycles with laparoscopic cystectomy of right endometriomas and 73 cycles with surgery for left side. Primary outcome measure was ovarian reserve and ovarian response. Secondary outcome measures were the implantation rate, clinical pregnancy rate, and live birth rate.

**Results:** There was no difference among two groups with regard to antral follicle count, number of oocytes retrieved, the dosage of gonadotropin, estradiol level on human chorionic gonadotropin day, good-quality embryos for transfer, and fertilization rate. The clinical pregnancy rate and live birth rate were similar between two groups, however, the implantation rate was significantly lower in the cycles with left side of ovarian endometrioma compared to right counterpart (10.1% vs. 20.2%;  $p = 0.015$ ).

**Conclusion:** There were no associations among the laterality of ovarian endometrioma, ovarian reserve and ovarian response in IVF/ICSI cycles. However, left ovarian endometrioma after laparoscopic cystectomy may impair implantation rate as compared to right ovarian endometrioma.

**Keywords:** Endometrioma, laparoscopy, IVF/ICSI

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### IS LAPAROSCOPIC SEGMENTAL COLORECTAL RESECTION EFFECTIVE TO IMPROVE THE PROBABILITY OF PREGNANCY IN POOR RESPONDERS WITH SEVERE ENDOMETRIOSIS UNDERGOING ICSI?

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**Objectives:** To evaluate the effect of radical surgery in cases of infiltrated bowel endometriosis in improvement in oocyte and embryo quality in poor responders undergoing intracytoplasmic sperm injection (ICSI).

**Design:** We have designed a prospective study.

**Materials and Methods:** From March 2009 to September 2013, 52 women with at least a 2 years diagnosed infertility and that had undergone ICSI treatments were analyzed, before surgery (Group 1) and after segmental bowel resection due to endometriosis (Group 2). All patients had a poor ovary response during treatment.

**Results:** Mean age was 34 years (range, 32-38). We had evaluated number of mature oocytes before and after surgery procedure as on day 2, cultured embryos on the basis of the number of blastomeres, blastomere size, fragmentation rate, and presence of multinucleated blastomeres. There were differences between groups in the number of oocytes retrieved, fecundation rate, number of embryos obtained, and pregnancy rate per transfer between groups. Table 1- Differences between women response in ICSI cycles before (Group 1) and after (Group 2) segmental bowel endometriosis resection

	Mean retrieved oocytes (n)	Fertilization rate	Embryos (n)
Group 1	2 (range 1-4)	56%	1 (range 0-3)
Group 2	5 (range 3-7)	78%	4 (range 2-6)

**Conclusion:** Insufficient evidence exists to recommend most of the treatments proposed to improve pregnancy rates in poor responders women with endometriosis. Currently, there is some evidence to suggest that removal of deep endometriosis with colorectal involvement before ICSI in infertile symptomatic patients, appear to improve the probability of pregnancy.

**Keywords:** Poor responders, endometriosis

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**EFFECTS OF POSTOPERATIVE ORAL CONTRACEPTIVE USE ON FERTILITY IN PATIENTS WITH ENDOMETRIOMA UNDERGOING LAPAROSCOPIC CYSTECTOMY.**

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**Objectives:** Postoperative oral contraceptive use (OC use) has received increasing attention as a potential strategy to prevent postoperative recurrence. In the present study, we examined the fertility of patients who discontinued OC use according to their wishes to have children

**Design:** A retrospective observational study of 162 women with endometrioma underwent laparoscopic cystectomy and postoperative OC use at our hospital between January 2005 and December 2011.

**Materials and Methods:** 8 women discontinued OC use because they wished to have children for reasons. We examined the patient characteristics, duration of OC use, recurrences during therapy, and fertility after discontinuation of the therapy.

**Results:** The mean ( $\pm$  SD) age of the patients at the time of discontinuation of OC use according to their wishes to have children was 25.3 ( $\pm$  2.8) years, with the mean r-ASRM score of 60.1 ( $\pm$  29.8). The mean maximum diameter of the endometrioma was 8.1  $\pm$  3.2 cm. Bilateral cysts were observed in 3 cases and a unilateral cyst in the remaining 5 cases. The mean duration of OC use was 13.4  $\pm$  4.8 months. Six patients (75%) became pregnant within 6 months after discontinuation of OC use.

**Conclusion:** The results of the present study suggested a positive effect of postoperative OC use on fertility in patients with endometrioma undergoing ovarian cystectomy, though the number of subjects was small. Further studies with a long-term follow up are required.

**Keywords:** fertility OC cystectomy

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### IMPORTÂNCIA DA LAPAROSCOPIA NA INVESTIGAÇÃO DA INFERTILIDADE E DETERMINAÇÃO DO PLANO TERAPÊUTICO.

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**Objectives:** Objetivo: Reexaminar a importância da laparoscopia na investigação de infertilidade e determinação do plano terapêutico.

**Design:** Desenho do estudo: Estudo coorte incluindo 237 pacientes com infertilidade > 12 meses

**Materials and Methods:** O fator masculino foi avaliado pela história médica e análise completa do sêmen. A avaliação da mulher incluiu rastreamento para doenças infecciosas, ultrassom transvaginal, parâmetros hormonais, histerossalpingografia e videolaparoscopia. O tratamento final foi decidido pelos achados laparoscópicos e qualquer modificação da proposta antes da laparoscopia considerou-se como mudança no tratamento.

**Results:** Resultados: Na laparoscopia cavidade pélvica estava normal em apenas 5.5% dos casos. Endometriose foi diagnosticada em 76.4%, aderências pélvicas em 17,2%, aderências ovarianas/periovarianas em 24,8%, aderências peritubárias em 15,2%, oclusão tubária unilateral em 21,1%, oclusão tubária bilateral em 5,5% e pequenas alterações tubárias como saculações, constrictões, enovelamento ou dobras em 46,3%. As intervenções cirúrgicas foram ablação/excisão de focos endometrióticas (74,6%), lise de aderências (27,4%), cistectomia de endometriomas (4,6%). Com os resultados pós-laparoscopia o plano de tratamento foi modificado em 35,8% dos casais.

**Conclusion:** Conclusões: Fator peritonal anormal, principalmente presença de endometriose, tem alta prevalência nas mulheres inférteis em Mato Grosso. A laparoscopia provê diagnóstico preciso do fator peritonal e altera o plano inicial de tratamento em pelo menos um terço dos casais.

**Keywords:** Laparoscopia, infertilidade, endometriose

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**AN UPDATED META-ANALYSIS ON THE USE OF LONG-TERM ADMINISTRATION OF GNRH-  
AGONISTS PRIOR TO IVF IN PATIENTS WITH ENDOMETRIOSIS**

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*No Abstract Available*

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### ECHOGRAFIC PREDICTIVE FACTORS OF URETERAL INVOLVEMENT IN DEEP ENDOMETRIOSIS

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**Objectives:** Evaluate which echografic signs are predictors ureteral involvement in women with deep infiltrating endometriosis (DIE).

**Design:** Retrospective observational study, from 2010 to 2013, of patients with deep endometriosis in the uterosacral ligament (USL) previously diagnosed by transvaginal echografic specialist who underwent laparoscopy treatment with histological diagnosis of endometriosis at gynecological endoscopy and endometriosis clinic at Santa Casa Medical School and private clinic, São Paulo – Brazil.

**Materials and Methods:** We evaluated 59 medical records of patients submitted to laparoscopic treatment of DIE. Analysed variables were: age, size and side of uterosacral ligament involvement, side ureter involvement, presence of ovarian endometriomas, performed laparoscopic ureterolysis, intraoperative and postoperative complications. The statistical analysis used significant  $p < 0.05$ .

**Results:** Fifty-nine patients were included in this study, all with DIE in the uterosacral ligament and all patients underwent laparoscopic surgery for DIE. The mean age was 36.1 years old. The prevalence of thickening uterosacral ligament in the echografic was 61.0% of cases bilateral, 23.7% on the left side, and 15.3% on the right side. The size of USL was associated with involvement of the homolateral ureter in the echografic, on the right side ( $p=0.039$ ) and on the left side ( $p=0.014$ ), and was associated with performed ureterolysis on both sides, the right ( $p=0.018$ ) and left ( $p=0.007$ ). Laparoscopic ureter intervention was ureterolysis in 49.15% (29/59) of patients. After surgery, 5 (8.47%) patients had complications, 2 (3.38%) transient urinary retention, 2 leakage and 1 (1.69%) stenosis of rectum.

**Conclusion:** Patients with DIE in the uterosacral ligament have a greater risk of having ureteral involvement (42.37%). The larger the size of USL the greater the chance of ureteral echografic changes and the need to perform ureterolysis.

**Keywords:** Endometriosis; Ureter; Laparoscopy

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**CLINICAL TREATMENT OF DEEPLY INFILTRATING ENDOMETRIOSIS WITH DIENOGEST: A PROSPECTIVE PILOT STUDY**

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**Objectives:** To evaluate the clinical treatment of deeply infiltrating endometriosis with dienogest, quantifying the frequency and intensity of pain symptoms and analysing adverse effects.

**Design:** Prospective study included 14 women with diagnosis of deeply infiltrating endometriosis that was made using surgical intervention, magnetic resonance imaging or transvaginal ultrasound; the patients were followed at the Gynaecology Department, University of Campinas (Unicamp).

**Materials and Methods:** All women received dienogest (2 mg once daily, orally) for 16 weeks. The variables considered were dysmenorrhoea, chronic pelvic pain, deep dyspareunia, and pain to evacuate and to urinate, measured by visual analog scale. For this analysis,  $P < 0,05$  was considered statistically significant. There were also gathered main adverse drug effects.

**Results:** The mean age was  $36 \pm 6,6$  years, 56% were nulliparous, mean body mass index was  $24,6 \pm 4,2$  and the initial age of symptoms was  $29,5 \pm 9,1$  years. There was a significant reduction after 4 months of dysmenorrhoea (7,8 to 1,1,  $p < 0,0001$ ), chronic pelvic pain (3,9 to 1,1,  $p = 0,03$ ) and deep dyspareunia (4,6 to 0,6,  $p = 0,004$ ). Although, the pain to evacuate and to urinate showed reduction in the scale, there was no statistical significance. About adverse effects, 56% presented headache, 31% breast pain and 43% libido decrease. All women exhibited irregular bleeding with the medication; however, it was not a motive for patients to interrupt the treatment.

**Conclusion:** The dienogest is an excellent drug for the treatment of deeply endometriosis. Despite the irregular bleeding, the medication provides a significant pain control. This effective management permits the clinical following of these patients, preventing the complications and the high morbidity of surgical procedures.

**Keywords:** Deeply endometriosis, dienogest

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**PRELIMINARY REPORT ON SURGICAL TREATMENT OF 191 CASES OF URETERAL  
ENDOMETRIOSIS**

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**Objectives:** Our goal is to describe the outcomes of laparoscopic surgery for ureteric endometriosis.

**Design:** Retrospective descriptive study of the outcomes for patients who underwent laparoscopic surgery due to endometriosis with ureteral involvement

**Materials and Methods:** Patients who underwent laparoscopic surgery due to endometriosis in which there was ureterolysis, resection with end-to-end anastomosis of ureter or re-implantation. The setting was in Department of Obstetrics and Gynecology, Strasbourg Hospitals, between June 2004 and June 2013. Data were collected from clinical file and included a telephone interview.

**Results:** We included 191 patients: 170 with ureterolysis, 20 with resection and end-to-end anastomosis and one re-implantation. Associated procedures were: 23 patients - segmental bowel resection, 37 - shaving of recto-vaginal nodule and 30 - resection of bladder endometriosis nodule. We founded 20 complications from which 4 uretero-vaginal fistula. Of the 20 patients 10 needed re-operation.

**Conclusion:** Ureteric involvement is usually asymptomatic, and therefore in patients with evidence of deep endometriosis it must be excluded. Laparoscopic treatment of ureteric endometriosis is feasible, but associated with non-negligible complications. Surgeons that perform this surgery should be able to treat them.

**Keywords:** Ureter endometriosis laparoscopy

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**AGGRESSIVE SURGICAL RESECTION OF SUBSEROAL UTERINE ENDOMETRIOSIS (SBSUE) BEFORE IN VITRO FERTILIZATION INCREASE THE RISK OF LATE GESTATION RUPTURE OF PREGNANT UTERUS AND UTERINE VEINS**

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**Objectives:** Laparoscopic surgery for deep infiltrative endometriosis (DIE) with extensive and complete resection of DIE lesions has been reported to be most effective. Although rare, aggressive surgical resection of SbsUE before in vitro fertilization increases the risk of cervical incompetence, life threatening late gestation rupture of pregnant uterus and uterine veins.

**Design:** Case reports of aggressive surgical resection of subserosal uterine endometriosis

**Materials and Methods:** Three women aged 35-38 years old, who had had 1-3 previous early miscarriages were evaluated for DIE and infertility. All women underwent pre-and-postoperative transvaginal bowel preparation (TVSBP). Due to the nature of DIE and the aggressiveness of SbsUE extensive DIE resections of the “endometriotic inner myometrium” contributed to outcome.

**Results:** Patients underwent extensive LSC resection of DIE including SbsUE. Prophylactic LSC cerclage was performed. TVSBP was carried out after LSC ≥3 months showing thin posterior cervix-uterine wall with cerclage suture intact. In vitro fertilization (IVF) treatment was then initiated. The women had no eventful 1st and 2nd trimester pregnancies except for a twin gestation. Spontaneous laboring began @30weeks and at 30-33weeks’ gestation they felt an increasing abdominal pain. All women were immediately hospitalized for evaluation of premature labor. Within a short time, they suddenly had an intra-abdominal hemorrhage, fetal distress and immediate cesarean section was performed. Four premature newborns were alive and did well. Uterine ruptures occurred in the posterior uterine wall of 2 women and rupture of uterine vein was noted in the twin gestation.

**Conclusion:** This report calls the attention to the fact that subserosal uterine endometriosis is an indicator of invasive of DIE proliferation. Aggressive surgical resection before contemplating spontaneous or after in vitro fertilization will possibly require cervical cerclage holding an increase risk of late gestation rupture of pregnant uterus and uterine veins.

**Keywords:** Subserosal uterine endometriosis

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**LAPAROSCOPIC NEPHRECTOMY IN THE MANAGEMENT OF SEVERE URETERAL  
ENDOMETRIOSIS WITH SILENT LOSS OF RENAL FUNCTION – A 5-CASE SERIES**

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**Objectives:** The main objective of this series is to report our experience on severe ureteral endometriosis causing nonfunctioning kidney, which management involved a laparoscopic nephrectomy.

**Design:** We performed a retrospective observational study

**Materials and Methods:** All patients with ureteral endometriosis and unilateral renal cortical loss, submitted to a laparoscopic surgical procedure including nephrectomy between January 2011 and October 2013 were included. Clinical presentation, imaging endometriosis findings, surgical management and short time postoperative outcome were evaluated.

**Results:** Five patients were identified, all referred for severe dyspareunia, dysmenorrhea and dyschezia. No urologic symptoms were present and physical examination was suggestive of deep posterior compartment endometriosis. For all cases, imaging documented nodular rectovaginal endometriosis, unilateral ureterohydronephrosis and significant renal cortical atrophy with negligible renal function. Extensive laparoscopic adhesiolysis, ureterolysis, unilateral nephrectomy and excision of rectovaginal nodule were performed. No symptom recurrences have been identified.

**Conclusion:** As illustrated by the presented cases, patients with renal function loss as a consequence of ureteral endometriosis frequently do not show urological symptoms. This emphasizes the need to evaluate urinary tract involvement in patients with deep endometriosis. Nephrectomy should be considered for significant renal impairment due to persistent ureterohydronephrosis.

**Keywords:** Ureteral-endometriosis, nephrectomy, laparoscopy

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### SUBSerosal Uterine Endometriosis (SbsUE) with Deeply Myometrial Invasion is a Marker of Aggressive Deeply Infiltrating Endometriosis (DIE) with Bladder and Bowel Involvement

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**Objectives:** To investigate whether an associated subserosal uterine endometriosis with deeply myometrial invasion is a marker of aggressive DIE with bladder and bowel involvement

**Design:** Observational study conducted in an University affiliated private infertility center between July 2009 and August 2013

**Materials and Methods:** 2081 infertile women with pelvic pain were evaluated for DIE with transvaginal ultrasound after bowel preparation (TVSBP) using a Voluson E8GE. Women who underwent laparoscopic (LSC) surgery of DIE lesions had histological confirmation. Severity of DIE was determined by at least 3 pelvic sites with bladder and/or bowel involvement.

**Results:** 291 women (35.6±4.3 years old; mean±SD) suffering from infertility for 1 to 6 years (2.9±1.8) underwent TVSBP and LSC. They underwent 2.8±1.6 previous IVF and 1.4±1.2 LSC attempts carried out by other colleagues before our studies and interventions. TVSBP identified 98 SbsUE, 31 SbsUE in the anterior compartment (AC) and 67 SbsUE in the posterior compartment (PC). All SbsUE were confirmed by LSC and histology. The mean number of DIE lesions was significantly greater in women presenting with SbsUE than those without it (3.68±1.92 vs. 1.79±1.1). Additionally, women who presented with SbsUE had extensive adhesions.

**Conclusion:** These findings indicate that the incidence of SbsUE is ~4.7% but the morbidity is overwhelmingly affecting both pelvic compartments. Furthermore, the surgical approach of SbsUE might be troubled by the lack of cleavage planes between the ill and the healthy tissue. The gynecologist must become acquainted with such condition.

**Keywords:** Subserosal uterine endometriosis

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**OUTCOMES IN THE LAPAROSCOPIC TREATMENT OF BLADDER ENDOMETRIOSIS: PRELIMINARY REPORT OF 60 CASES**

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**Objectives:** To report the performance of the different techniques in bladder endometriosis. Pain scores, complications and recurrence are described.

**Design:** Retrospective study of patients with bladder endometriosis managed at the University Hospitals of Strasbourg between January 2006 and June 2013.

**Materials and Methods:** Only cases of deep infiltrating endometriosis (DIE) were included (detrusor invasion). The groups were divided in partial cystectomy (PC) and partial-thickness excision (PTE).

**Results:** Forty-two patients (70.0%) underwent PC, and the remaining patients underwent PTE. The pain relief was reduced in both groups. No bladder recurrences were found. Major complications developed in 12 PC patients, 11 of them primarily related to bowel resection or ureteral surgery. Of the 12 patients 7 complications were managed surgically.

**Conclusion:** Laparoscopic management is feasible and associated with reduction of pain and low recurrence rates. As expected, complications were associated with bigger resections and, in our series, only to cases of partial cystectomy. Interestingly, the majority of complications were primarily related to associated procedures.

**Keywords:** Endometriosis; bladder; surgery

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### MANAGEMENT OF DEEP ENDOMETRIOSIS WITH COLORECTAL INVOLVEMENT: WHAT SURGICAL OPTIONS?

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**Objectives:** To report the results of different surgical techniques in the management of patients with deep infiltrating endometriosis and colorectal involvement.

**Design:** We performed a retrospective observational study.

**Materials and Methods:** We reviewed all cases of deep endometriosis with colorectal involvement submitted to laparoscopic surgery between June 2009 and October 2013. Patients underwent either parietal shaving of the bowel wall, discoid resection or segmental resection depending on the extension of intestinal involvement. We analyzed the operative complications and clinical outcomes.

**Results:** From the 81 women included in the analysis, 74 (91.4%) had a superficial parietal shaving of the bowel wall, 3 (3.7%) underwent a discoid resection and 4 (4.9%) underwent a segmental colorectal resection. The presence of deep endometriosis was confirmed in all specimens. In the parietal shaving group there was 1 case of superficial rectal perforation resolved intra-operatively and 1 case of bowel obstruction do to adhesive peritonitis at the 14th post-operative day. There were two cases of pain recurrence with need for a second surgery. At the last follow-up evaluation we registered a mean dyschezia improvement of 4 points (0 to 10 scale), and dyspareunia of 3 points. The mean follow-up period was 12.3 months.

**Conclusion:** Laparoscopic colorectal surgery in deep infiltrating endometriosis is safe and feasible, providing a durable symptomatic control and a low reoperation rate, when performed by an experienced team.

**Keywords:** Deep endometriosis laparoscopy

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### IS OVARIAN ENDOMETRIOMA A MARKER OF THE EXTENSION OF DIE?

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**Objectives:** To verify the association between the presence of unilateral or bilateral ovarian endometrioma and the number of areas affected by deep infiltrating endometriosis (DIE).

**Design:** It is a seccional study

**Materials and Methods:** 138 women in reproductive age underwent laparoscopic treatment of DIE from 2011 to 2013. They were divided in groups according to side of endometrioma. All visible lesions were considered endometriosis only when confirmed by histopathology. The total number of lesions was obtained by the sum of the affected sites.

**Results:** Results: The median age of patients was 35.0 years (minimum – maximum: 19-52). Ovarian endometriomas were present in 92 patients (66.7%). In 16 patients (11.6%) they were on the right side, in 21 (15.2%) on the left side and in 55 (39.9%) bilateral. The number of affected sites by DIE was not statistically different (P .228) between patients with ovarian endometrioma (median 5.0, min-max: 1-11) and without ovarian endometrioma (median 4.0, min-max: 1-12). The number of affected sites by DIE was also not different (P .468) between the groups with unilateral endometrioma (median 6.0, min-max: 1-10), bilateral endometrioma (median 5.0, min-max: 1-11) and without endometrioma.

**Conclusion:** Ovarian endometrioma is highly associated with DIE but is not predictive of the extension of the disease.

**Keywords:** Endometriosis endometrioma location

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### DO ENDOMETRIOMAS REALLY PREDICT ENDOMETRIOSIS SEVERITY?

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**Objectives:** Evaluate whether the presence of endometrioma was associated with endometriosis severity or any specific anatomical site.

**Design:** Retrospective evaluation of clinical and surgical data of 150 consecutive patients with histologically proven endometriosis.

**Materials and Methods:** Women were divided into two groups: endometrioma (n=38) and without endometrioma (n=112). Outcomes recorded were: Clinical (presence of infertility, pelvic pain, altered pelvic exam) and surgical (ASRM stage and score, endometriotic lesion location, presence of adhesions and surgical complications).  $p < 0.05$  was considered statistically significant for all analyses.

**Results:** Chronic pelvic pain was the main surgical indication in both groups (82%) followed by pelvic mass. 39% (n=59) had not been previously treated whereas 21% (n=32) had previously undergone both surgical and medical treatments. Most women were infertile (n=69;45%) and 29%(n=45) had never attempted pregnancy. When both groups were compared, the women without endometrioma complained more of dyschezia ( $p=0,016$ ) and had been treated before ( $p=0,002$ ). They also exhibited more alterations in the pelvic exam (pouch of douglas) ( $p=0,042$ ) higher ASRM score ( $p=0,0001$ ), adnexal adhesions ( $p=0,000$ ), more infiltrative disease in the pouch of douglas/rectovaginal septum ( $p=0,001$ ) and deeply infiltrative endometriosis ( $p=0,017$ )

**Conclusion:** Women without endometrioma presented with increased disease severity represented by more clinical symptoms (dyschezia), alterations in the pelvic exam, more adnexal adhesions, higher ASRM score as well as more infiltrative disease.

**Keywords:** Endometrioma, surgery, staging

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**CORRELATION BETWEEN THREE-DIMENSIONAL (3D) ANORECTAL ULTRASONOGRAPHY FINDINGS AND GASTROINTESTINAL COMPLAINTS IN PATIENTS WITH DEEP ENDOMETRIOSIS**

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**Objectives:** To correlate the severity of intestinal involvement by endometriotic lesions on 3D anorectal ultrasonography (3D US) with gastrointestinal complaints in patients diagnosed with deep endometriosis.

**Design:** Conducted at the Department of Colorectal Surgery of the Genesis Hospital from March 2008 to August 2011, this prospective study included 121 women (mean age: 34.59 years) with deep endometriosis referred to the outpatient gynecology service due to gastrointestinal complaints.

**Materials and Methods:** The patients were submitted to 3D US in 66 women (54.55%) lesions extended as far as the perirectal fat (Group I), while 55 (45.45%) had lesions infiltrating the rectal layers (Group II). The findings were compared with the clinical complaints.

**Results:** Group I displayed endometriotic foci measuring 4.24 cm and the distance from the lesion to the puborectalis muscle was 1.83 cm. Symptoms included cyclical rectal pain (39.39%) and constipation (42.42%). Group II displayed endometriotic foci measuring 2.18 cm and the average distance from the lesion to the puborectalis muscle was 4.22 cm. Symptoms included cyclical rectal pain (41.81%) and constipation (50.9%).

**Conclusion:** The severity of intestinal involvement by endometriotic lesions on 3D anorectal ultrasonography (3D US) was not correlated with gastrointestinal complaints in patients diagnosed with deep endometriosis.

**Keywords:** Ultrasonography, deep endometriosis

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### BLADDER ENDOMETRIOSIS AND DIENOGEST: CASE SERIES AND LITERATURE REVIEW

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**Objectives:** To present the experience with the use of dienogest in management of invasive bladder endometriosis.

**Design:** An international multicenter collaboration involving three sites specializing in endometriosis management. Cases of bladder nodules where dienogest was used in the management alone or in combination with surgical excision were collected.

**Materials and Methods:** A common intake sheet was circulated for uniformity in data collection. All the information was anonymized. The intake sheet for individual patients was completed and sent back to a common centre for analysis. Total of ten cases were collected from three centres.

**Results:** All the patients had a single bladder nodule ranging from 18 mm to 41 mm in the longest dimension. Medical management with dienogest was combined with surgery in eight out of ten cases, surgery was not performed in two cases. When used alone more than 50% reduction in size of the bladder nodule (4.0 cm to 1.5 cm and 3.3x3.0x2.7 cm to 2.8x2.3x1.0 cm) as well as complete resolution of symptoms was seen in both the cases with 9-16 months of use. Dienogest when prescribed preoperatively provided significant or complete resolution of symptoms in all but one case where symptomatic improvement was minimal. None of the patients experienced any major adverse drug reactions and minor side effects included headache or irregular bleeding.

**Conclusion:** Dienogest may be an effective and safe medical alternative, providing symptomatic and therapeutic benefit in cases of invasive bladder endometriosis prior to surgery or in place of surgery when indicated.

**Keywords:** Diagnosis Endometriosis Imaging

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**RELATION BETWEEN LOCATION OF DIE AND PRESENCE OF OVARIAN ENDOMETRIOMA.**

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**Objectives:** To verify the relation between sites affected by deep infiltrating endometriosis (DIE) and the presence of ovarian endometrioma.

**Design:** It was a seccional study

**Materials and Methods:** 140 women in reproductive age underwent laparoscopic treatment of DIE from 2011 and 2013. Lesions were considered endometriosis when confirmed by histopathology. Patients had the location of DIE identified and divided in groups according to the presence or absence of endometrioma. Chi-square test was used.

**Results:** The median age of patients was 35.0 years (minimum – maximum: 19-52). The prevalence of ovarian endometrioma was 65.7% (92 patients). The most affected site by DIE was the uterosacral ligament (82.9%). The presence of endometrioma is related to the presence of lesions of DIE in rectosigmoid (P .035). Patients with endometriomas are more likely to have lesion in the rectosigmoid.

**Conclusion:** Patients with deep infiltrating endometriosis and ovarian endometrioma should be investigated for lesion in the rectosigmoid.

**Keywords:** Endometriosis endometrioma location

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**IS RECTOSIGMOID ENDOMETRIOSIS A RISK FACTOR FOR THE INVOLVEMENT OF THE APPENDIX IN WOMEN WITH DEEP INFILTRATING ENDOMETRIOSIS?**

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**Objectives:** To evaluate the prevalence of appendix endometriosis in patients with Deep infiltrating endometriosis (DIE) with and without rectosigmoid endometriosis.

**Design:** Prospective and case control study.

**Materials and Methods:** Retrospective analysis of 85 patients undergoing laparoscopy for DIE. Patients with clinical suspicion of DIE underwent imaging with transvaginal ultrasonography and MRI. Appendix were evaluated during surgery. Endometriosis was confirmed by histopathology. Statistical analysis was performed with SPSS 20.0. We used the Fisher exact test with  $p < 0.05$ .

**Results:** Of the 85 patients undergoing laparoscopy for DIE, appendix endometriosis was found and confirmed by histopathology in 19 cases (22.4 %). Rectosigmoid endometriosis was observed in 50 cases (58.8 %) versus 35 cases (41.2 %) with other forms of the disease. Of the 50 patients with endometriosis of the rectosigmoid, involvement of the appendix occurred in 17 cases (34 %) versus 2 cases (5.7 %) in 35 patients without rectosigmoid endometriosis. Appendix endometriosis was statistically more prevalent in patients with DIE and rectosigmoid lesions than patients with DIE without rectosigmoid lesions ( $p = 0.003$ ). The odds ratio calculated was 8.5 (OR = 8.5, CI - 95 % = 1.8 to 39.7).

**Conclusion:** Presence of rectosigmoid endometriosis in patients with DIE is associated with increased risk for appendix endometriosis. Patients with rectosigmoid endometriosis have 8.5 times more likely to involvement of the appendix than those with DIE without rectosigmoid lesions. Systematic examination of the appendix in patients and rectosigmoid lesions is mandatory.

**Keywords:** Endometriosis, appendix, rectosigmoid

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### MAP FOR LOCATION OF ENDOMETRIOSIS

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**Objectives:** To develop and test a visual map that corresponds practically and objectively to the anatomical areas affected by endometriosis.

**Design:** Original Idea to help the surgeon at surgery time.

**Materials and Methods:** The diagram is a graphic representation of all sites of endometriosis. It should be filled at the time of surgery indication, namely with all the propaedeutics completed and the surgeon having already identified the locations affected by the disease.

**Results:** The surgeon with the diagram at the time of surgery, has a special tool that concentrates all the details of the case. This MAP can be checked at any time in surgery and may guide the surgical team, even in the absence of medical records. Postoperatively, the MAP allows an evaluation of our propaedeutics in cases of endometriosis, comparing all the sites identified in the diagram preoperatively with the surgical findings.

**Conclusion:** Therefore, the MAP becomes an important tool for the physician self-evaluation, both on physical examination, as in the imaging.

**Keywords:** Endometriosis, mapping, staging

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### LAPAROSCOPIC SEGMENTAL BOWEL RESECTION FOR DEEP PELVIC ENDOMETRIOSIS: 380 CASES FOLLOWED DURING 4 YEARS

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**Objectives:** The aim of this study was to assess the outcomes and clinical data after treating symptomatic women with deep infiltrating intestinal endometriosis by laparoscopic segmental bowel resection in a referral private clinic.

**Design:** We have designed a prospective study.

**Materials and Methods:** Between July 2009 and September 2013, we prospectively evaluated 380 women who underwent segmental bowel resection for endometriosis. All women were submitted to transvaginal sonography with bowel preparation before surgery to evaluate size and wall infiltration of lesions in retosigmoid, and all of them were submitted to laparoscopic colorectal resection.

**Results:** Mean patient age at surgery was 32.8 years (range: 24–41). Two hundred eight nine women (76%) had at least one previous surgery for endometriosis. Primary symptom at initial consultation was dysmenorrhea in 365 patients (96%); non menstrual pelvic pain in 205 (54%), dyspareunia in 243 (64%), primary or secondary infertility in 262 (69%), and 361 women had any bowel symptom during menstruation. Blood loss during surgery was not significant and mean hospital stay was 4 (3-5) days. There were no conversions to laparotomy. There was a positive effect of surgical excision on patient quality of life.

**Conclusion:** Segmental laparoscopic bowel resection for deep intestinal endometriosis in symptomatic women significantly reduces pain and improves quality of life. Also it is safe and effective in resolving pain and dysfunctional symptoms.

**Keywords:** Deep endometriosis, laparoscopy

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**DISCOID RESECTION NEW TECHNIQUE: DOING MORE BY DOING LESS**

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**Objectives:** To describe an alternative technique for bowel endometriosis treatment with bowel shaving followed by discoid resection.

**Design:** To describe a series of patients treated with bowel endometriosis by shaving followed by discoid resection.

**Materials and Methods:** To compare patients who had bowel shaving followed by bowel discoid resection to patients who had segmental bowel resections between January 2010 and September 2013. Surgical technique was chosen by surgeon. We intend to describe surgical outcomes.

**Results:** In this paper we intend to describe: population characteristics, proportion of infertile patients, number of prior surgeries related to endometriosis, medical treatment prior to surgery, pain evolution (dysmenorrhea, dyspareunia, chronic pelvic pain, dysuria and dysphasia), functional symptoms (bladder and bowel), complications (intra-operative, post-operative), bowel endometriosis recurrence, pregnancy rate and general outcomes

**Conclusion:** Discoid resection technique brings the benefit of an anterior wall resection with minimum mesosigmoid dissection but is limited by the size of the circular stapler. Combining the shaving technique to the discoid resection it is possible to remove bigger nodules without the necessity for the segmental resection.

**Keywords:** Bowel Endometriosis Treatment

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### DEEP ENDOMETRIOSIS AND BILATERAL URETERAL OBSTRUCTION: A CASE REPORT OF LAPAROSCOPIC TREATMENT

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**Objectives:** To relate a case of deep endometriosis with bilateral ureteral obstruction in a patient with moderate dysmenorrhea and surgery treatment totally laparoscopic.

**Design:** A case report of bilateral ureteral endometriosis, consisting on a 33-year-old female

**Materials and Methods:** The patient has been submitted to laparoscopic ureteroneocystostomy and vesicopsoas hitch with retosigmoidectomy, allowing the preservation of the renal unit.

**Results:** This patient with 33-year-old female, 1Gab1, with dismenorrhea using continuous oral contraception and chronic bilateral hydronephrosis due to extrinsic compression has a Magnetic resonance: an important bilateral hydronephrosis, infiltrating endometriosis retrocervical that extends up to the vaginal vault and parametrium, obstructing and invading the rectosigmoid and ureters bilaterally with extension of 4.2cm. The patient had a history of renal colic and double-J catheter for a month. No intraoperative and postoperatively complications occurred. She had an indwelling Foley catheter for approximately 2 weeks postoperatively.

**Conclusion:** The patient underwent laparoscopic ureteroneocystostomy and vesicopsoas hitch with retosigmoidectomy and no complications occurred.

**Keywords:** Endometriosis, bilateral obstruction

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**PREGNANCY IN PATIENTS WITH RETROCERVICAL AND/OR DEEP ENDOMETRIOSIS: PARCIAL RESULTS**

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**Objectives:** Objective: To analyse the obstetric outcome in patients with diagnose of retrocervical and/or deep endometriosis

**Design:** Design: this is a prospective coorte study

**Materials and Methods:** Matherial and methods: Twelve patients referred with suspected endometriosis, between march 2008 and july 2013. The protocol was completed with clinical data, image and laboratory results, treatment and follow-up. The patients were evaluated by the same gynecologist (SP), and six of them examined by the same professional image (CM).

**Results:** Results: The age range 26-39 years old, all nulliparous, six of them with pelvic pain. Five patients had just undergone laparoscopies. CA-125 range between 8,7 and 32. Deep endometriosis involving muscular of rectosigmoid was seen in seven patients by image (ultrasound - US - and/or magnetic ressonance image - MRI). In the others patients (five), the image was retrocervical nodule without rectosigmoid invasion. Seven patients underwent surgery. Four patients became pregnant and have children (two by two times), three wanting to concieve and five not to be pregnant now, using contraceptive. The four patients who were pregnant, only one underwent surgery.

**Conclusion:** Conclusions: From twelve nulliparous patients, seven want to be pregnant still now, and four had six children.

**Keywords:** Deep endometriosis, retrocervical

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**CORRELATION BETWEEN THREE-DIMENSIONAL (3D) ANORECTAL ULTRASONOGRAPHY, VIDEOLAPAROSCOPY AND CLINICAL FINDINGS IN PATIENTS WITH DEEP ENDOMETRIOSIS**

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**Objectives:** The purpose of this study was to evaluate the correlation between 3D anorectal ultrasonography (3D US), videolaparoscopy (VL) and clinical findings in patients with deep endometriosis.

**Design:** This prospective study included 118 women (mean age: 34.39 y) with deep endometriosis referred Department of Colorectal Surgery due to gastrointestinal complaints and enrolled between March 2008 and August 2011. All patients were submitted to clinical evaluation, 3D US and, posteriorly, to VL

**Materials and Methods:** The evaluated complaints included pain in the right iliac fossa, low abdominal pain, cyclical rectal pain, tenesmus, noncyclical constipation, dyspareunia and infertility. Sixty six patients with 3D US findings suggestive of intestinal involvement by foci of endometriosis were submitted to multidisciplinary laparoscopic surgery by a team of gynecologists and coloproctologists.

**Results:** Forty nine presented dyspareunia, 35 noncyclical constipation, 46 cyclical low abdominal pain, 27 cyclical rectal pain and 3 tenesmus. Of these, 28 presented dyspareunia associated with noncyclical constipation, 36 dyspareunia associated with low abdominal pain, 17 noncyclical constipation associated with cyclical rectal pain, and 18 low abdominal pain associated with cyclical rectal pain

**Conclusion:** Patients with deep endometriosis undergoing investigation for infertility and with gastrointestinal complaints should be submitted to 3D US by a colorectal surgeon to define if multidisciplinary surgery is necessary.

**Keywords:** Deep endometriosis, videolaparoscopy

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**IN VITRO STUDY OF TWO NATURAL COMPOUNDS FOR ENDOMETRIOSIS TREATMENT: RESVERATROL AND EPIGALLOCATECHIN GALLATE (EGCG). IMPLICATIONS OF NF- $\kappa$ B PATHWAY.**

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**Objectives:** We study the in-vitro effect of two natural polyphenols, resveratrol and EGCG on endometrial cells proliferation and their possible molecular mechanism of action through the NF- $\kappa$ B pathway. Our previous studies shown that both compounds have a strong antiproliferative and proapoptotic activity both in-vivo and in-vitro in experimental endometriosis.

**Design:** Endometrial carcinoma cell line (ECC-1) was cultured according to standard protocols in RPMI 5% fetal bovine serum. After 48 hours, cells were harvested and 24 hours later were stimulated with different doses of resveratrol (50 and 100 $\mu$ M) or EGCG (20 and 40 $\mu$ M) for 24 hours.

**Materials and Methods:** Cell proliferation was assessed using the MTS reduction kit. Nuclear and cytoplasmic extractions were performed by NE-PER kit. The activation of NF- $\kappa$ B (p65) was evaluated using the DNA-binding-Elisa TransAM kit and the levels of total I $\kappa$ B $\alpha$  in cytoplasmic fractions were assessed by Western Blot.

**Results:** We found that both resveratrol and EGCG induced an inhibition of proliferation in ECC-1 ( $p < 0.01$ ). Moreover, the levels of activated NF- $\kappa$ B (subunit p65) measured in nuclear fractions from ECC-1 cells were decreased by both treatments. EGCG at both assayed doses and Resveratrol 100  $\mu$ M reduced these levels compared to baseline ( $p < 0.001$ ,  $p < 0.05$  and  $p < 0.01$  respectively). NF- $\kappa$ B is known to be controlled upstream by I $\kappa$ B $\alpha$ , which sequesters NF- $\kappa$ B in the cytoplasm. Consistently, we observed an increase of the total I $\kappa$ B $\alpha$  levels in cytoplasmic fractions, with the highest assayed dose of resveratrol compared to baseline ( $p < 0.05$ ). In addition, the lowest assayed dose of EGCG was able to induce an increase in total cytoplasmic I $\kappa$ B $\alpha$  levels ( $p < 0.05$ ).

**Conclusion:** Based on our results, we suggest that suppression of NF- $\kappa$ B activation by resveratrol and EGCG may be a possible mechanism that explains the inhibition of endometrial proliferation. The integration of these results with our previously published ones encourages us to investigate these compounds as novel strategies to treat endometriosis.

**Keywords:** Resveratrol, EGCG, NF- $\kappa$ B.

## Poster - Medical treatment

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### SODIUM BUTYRATE (NABU) CAUSES REGRESSION OF ENDOMETRIOTIC IMPLANTS IN A RAT ENDOMETRIOSIS MODEL: A PRELIMINARY STUDY

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**Objectives:** To determine the effects of sodium butyrate (NaBu) on the endometriotic lesions in a surgically induced rat endometriosis model

**Design:** This is a prospective, randomized, controlled, experimental study carried out at the Experimental Research Center of Yeditepe University (YUDETAM).

**Materials and Methods:** Endometriosis was surgically induced in oophorectomized nulligravid Wistar - Hannover albino rats. 25 mg/kg/day NaBu was administered for two weeks starting at the end of the 2nd week. Estrogen was administered throughout the study. The lesions were measured and biopsies were done at the 2nd, 4th, and 6th weeks.

**Results:** The mean volumes of the endometriotic foci were 184,4±84,4 mm<sup>3</sup>, 60,79±34,12 mm<sup>3</sup>, and 25,98±46,88 mm<sup>3</sup>, and histopathological scores were 2±0,7071, 1,518±0,9282 and 1,441±1,345 in the sodium butyrate group at the end of the second, fourth, and sixth weeks, respectively. The mean volumes of the endometriotic foci were 132,7±185,2mm<sup>3</sup>, 148,6±216,9 mm<sup>3</sup>, and 220,3±387,7mm<sup>3</sup>, and histopathological scores were 1,533±0,8958, 1,3±1,334 and 1,7±1,082 in the control group at the end of the second, fourth, and sixth weeks, respectively. In the NaBu group endometriotic mean volumes decreased significantly at the second, fourth, and sixth weeks.

**Conclusion:** NaBu causes significant decrease in the volumes of the endometriotic foci compared to control group. NaBu seems to be a novel agent in the treatment of endometriosis

**Keywords:** Sodium Butyrate, endometriosis

Poster - Medical treatment

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**PHARMACOKINETICS OF ELAGOLIX, AN ORAL GONADOTROPIN-RELEASING HORMONE (GNRH) ANTAGONIST IN HEALTHY PREMENOPAUSAL HAN CHINESE AND JAPANESE FEMALE SUBJECTS**

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**Objectives:** To assess the pharmacokinetics and safety of single and multiple doses of elagolix in healthy premenopausal Japanese and Han Chinese females.

**Design:** This was a double-blind, randomized, placebo-controlled study. Twenty Japanese subjects and twenty Han Chinese subjects were randomized to receive multiple doses of elagolix 150 mg once daily (QD), 200 mg twice daily (BID) or placebo for 7 days.

**Materials and Methods:** Single and multiple-dose intensive pharmacokinetic blood samples for elagolix assay were collected. Pharmacokinetic analyses were conducted using Pharsight Phoenix WinNonlin and statistical analyses were performed using SAS. Safety was evaluated through adverse event monitoring, vital signs, physical examination, ECG, and laboratory tests assessments.

**Results:** Elagolix pharmacokinetics were similar between Japanese and Chinese subjects. Elagolix exposure was dose proportional. Mean elimination half-lives were similar, with minimal accumulation in both populations after multiple dosing. These findings were consistent with PK data generated in US (Western) adult healthy premenopausal women. Both elagolix regimens were generally well-tolerated. Nine of 16 (56%) Japanese and 9/16 (56%) Chinese subjects receiving elagolix reported at least one treatment emergent adverse events (AEs), compared to 1/4 (25%) Japanese and 4/4 (100%) Chinese subjects who received placebo. The AEs reported by more than one subject were presyncope, urinary tract infection and constipation and were assessed by the investigator as probably not related to elagolix. No clinically significant abnormal ECG findings were reported.

**Conclusion:** Elagolix pharmacokinetics were linear and similar between Japanese and Han Chinese subjects and was consistent with data from US Western subjects. Both elagolix dose regimens (150 mg QD and 200 mg BID) were generally well-tolerated by Japanese and Han Chinese subjects.

**Keywords:** Elagolix, GnRH, antagonist

Poster - Medical treatment

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**DESIGN OF THE TERRA STUDY: A PHASE-2 DOSE RESPONSE STUDY WITH ASP1707 A NEW ORAL GNRH ANTAGONIST FOR THE TREATMENT OF ENDOMETRIOSIS ASSOCIATED PELVIC PAIN**

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**Objectives:** To investigate efficacy and dose-response of 4 dose groups ASP1707 relative to placebo in reduction of endometriosis associated pain after 12 weeks treatment in patients with moderate to severe endometriosis pain and to assess safety and effect on Bone Mineral Density (BMD) after 24 weeks treatment, with leuprorelin as control.

**Design:** Multinational, double-blind, randomized, parallel-group, placebo-controlled phase 2 study for 12 weeks, followed by a double-blind extension up to 24 weeks without placebo control. One additional group will be treated with leuprorelin as active control for BMD assessment. Sample size is 84 subjects per group.

**Materials and Methods:** Patients with moderate to severe endometriosis related pelvic pain based on a Numeric Rating Scale are selected. During the study, subjects will record daily pelvic pain scores, bleeding days and amount of vaginal bleeding in an electronic diary.

**Results:** A phase 2 protocol has been written (ref. ClinicalTrials.gov NCT01767090) and initiated and is planned to enroll a total of 504 subjects (84 subjects per treatment group). Recruitment started in December 2012 in the following countries: Belgium, Bulgaria, Germany, Hungary, Japan, Poland Romania, Ukraine and UK. As of October 1, 2013 86 patients have been randomized. Recruitment is ongoing and expected to be finalized by Q2 2014. The poster will contain blinded baseline data of the patients recruited by 1 April 2014. Results are expected at the end of 2015.

**Conclusion:** ASP1707 is a promising new treatment for endometriosis currently in phase-2. Recruitment of this phase 2 study was started in December 2012 and is expected to be completed by Q2 2014. Results of the study are planned to be published in 2015.

**Keywords:** Endometriosis; Pain; GnRH-antagonist

Poster - Medical treatment

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**IN VITRO EFFECTS OF A NANOCOMPOSITE CONTAINING COPAIFERA LANGSDORFFII OLEORESIN ON STROMAL CELLS OF EUTOPIC ENDOMETRIUM AND ENDOMETRIOTIC LESIONS**

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**Objectives:** To investigate the effects of a nanocomposite containing the copaiba (*Copaifera langsdorffii*) oilresin on human eutopic endometrium stromal cells obtained from endometrial biopsies of patients with and without endometriosis, and human stromal cells from biopsies of ovarian capsule endometriotic lesions. Endometrial cell behavior is important to understand endometriosis development.

**Design:** Endometriosis treatment is principally aimed at down-regulating the ovarian estrogen production that is often associated with side effects. This is an in vitro study of endometriotic stromal cells treated with copaiba oilresin that has therapeutic properties in folk medicine, such as anti-inflammatory and antitumoral activities.

**Materials and Methods:** The oilresin was obtained from *Copaifera langsdorffii* trunk and a nanocomposite system was developed. Human eutopic and ectopic endometrium primary stromal cells were established, characterized and treated with 50µg/mL of the copaiba nanocomposite in order to evaluate its effects on cytotoxicity, cell morphology and proliferation, death induction and signaling pathways.

**Results:** Homogeneous stromal cell populations that expressed CD10, vimentin, fibronectin, type IV collagen and chondroitin sulfate were established and incubated with 50, 150 and 300µg/mL of this nanocomposite during 48h. Inhibition of cell viability and proliferation in a dose-dependent manner was showed, mainly in the stromal cells from endometriotic lesions. Moreover, the cell cultures were incubated with 50µg/mL of nanocomposite for 24, 48 and 72h and a cell viability reduction and an increased LDH release were observed in a time-progressive manner, also mainly in cultures from endometriotic lesions. In addition, morphological cell changes were observed in the cultures treated with 50µg/mL during 24h, excepting endometrium stromal cells from patients without endometriosis.

**Conclusion:** These preliminary results showed that this copaiba nanocomposite can negatively affect the endometriotic stromal cell behaviors and stimulate further studies of its effects on endometriosis. The results also suggest a potential candidate of a new phytotherapeutic agent on the management of this pathology.

**Keywords:** Endometriosis; nanocomposite; treatment

Poster - Medical treatment

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**FREQUENCY OF ENDOMETRIOSIS AT LAPAROSCOPIC SEARCH AFTER UNSUCCESSFUL MEDICAL TREATMENT FOR CHRONIC PELVIC PAIN**

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**Objectives:** To evaluate the efficacy of clinical treatment while inducing amenorrhea for chronic pelvic pain and which was the frequency of pelvic endometriosis at women who didn't have a successful response to the treatment.

**Design:** A prospective study from October 2007 to June 2013 where women with chronic pelvic pain and without clinical or ultrasound evidence of gynecologic pathologies, were treated with continuous hormonal therapy to induce amenorrhea and were followed every two months until 6 months.

**Materials and Methods:** The intensity of the pain was determined by Analogic Visual Scale during the initial medical evaluation and every 2 months. After 6 month follow-up, persistence and intensity of chronic pelvic pain were determinant to search for endometriosis and women with persistent pain went to laparoscopy.

**Results:** Eighty-five women completed 6 month follow-up. Eighty (94,1%) compleined of dysmenorrhea and initial VAS' score was 8,46. Dyspareunia was reported by 66,7% with inicial score of 7,0. And acyclic pelvic pain had 72,9% of frequency with 6,72 score. After six month, the pain's scores were: 1,69; 4,34 and 3,34, respectively. When initial and final scores were compared, there was difference between all symptoms' scores: dysmenorrhea ( $p < 0,0000001$ , IC: 6,04– 7,42), dyspareunia ( $p = 0,0001$ , IC: 1,31– 4,00) and acyclic pelvic pain ( $p < 0,0000001$ , IC: 2,30– 4,46). Thirty-one (36,5%) women presented persistent pain and were submitted to laparoscopy. Thirteen (41,9%) had endometriosis, 9 (29%) normal pelvis, 4 enlarged pelvic veins, 4 isolated adhesions and one inflammatory disease suspicion. All endometriosis lesions were peritoneal and superficial but one, that infiltrated bladder peritoneum.

**Conclusion:** Although dysmenorrhea, dyspareunia and acyclic pain scores had shown significative improvement with medical induced amenorrhea, about 35% of women had persistent chronic pelvic pain triggering the laparoscopic search for the pain cause. And almost 42% of them presented endometriosis at surgery, mostly superficial and peritoneal.

**Keywords:** Pelvicpain, endometriosis, laparoscopy

## Poster - Medical treatment

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### TALIDOMIDA EFFECT ON CELL PROLIFERATION EVALUATED BY PCNA LABELLING IN ENDOMETRIOSIS EXPERIMENTAL MODEL IN RATS.

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**Objectives:** To evaluate the efficacy of talidomida in different concentrations for treatment purpose in induced endometriosis in an experimental model in rats, by characterizing the cell proliferation pattern, by PCNA immunolabelling, in topic and ectopic endometrial tissue.

**Design:** Prospective experimental model using a rat experimental model. Fifteen adult Wistar rats were submitted to endometriosis induction by fixation of two fragments of the uterine left horn (5x5mm) in the abdominal wall. After four weeks the animals were divided in three groups: Group I(control), Group II(10mg/kg/day) and Group III(1mg/kg/day).

**Materials and Methods:** After this period all rats were sacrificed, the endometriosis implants were removed. Tissue processing included hematoxilin-eosin staining and immunolabelling for PCNA in order to evaluate cell proliferation, of topic and ectopic tissue. Cell Proliferation Index(CPI) was also calculated based on the number of labeled cells in each 1000 counted cells.

**Results:** Group I presented grater CPI mean ( $0.248 \pm 0.0513$  and  $0.178 \pm 0.046$  in gland and stroma, respectively) than groups II and III ( $0.088 \pm 0.009$  and  $0.080 \pm 0.021$  for GII gland and stroma ( $p < 0.001$ ) and  $0.0945 \pm 0.0066$  and  $0.075 \pm 0.018$  for GIII gland and stroma ( $p < 0.001$ ), respectively). When groups II and III were compared there was no difference in CPI.

**Conclusion:** Talidomida appeared to be efficient in reducing the CPI of endometriosis implants in rats experimental model in both doses of 1 and 10mg/kg/dia

**Keywords:** Endometriosis, talidomida, proliferation

Poster - Medical treatment

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**THE IN VITRO EFFECT OF DROSPIRENONE ON NORMAL ENDOMETRIAL AND ENDOMETRIOTIC STROMAL CELLS.**

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**Objectives:** Drospirenone (DRSP) is used as a progestin in contraceptives. Many progestins induce decidualization on normal endometrial stromal cells (NES) and inhibit proliferation of endometriotic stromal cells (ESC), while those effects of DRSP remain unknown. The aim of this study was to evaluate the effect of DRSP on NES and ESC.

**Design:** The study was approved by IRB. Endometrial and endometrioma tissues were obtained from patients undergoing surgery after obtaining written informed consents. NES were treated with DRSP and/or estradiol, and decidualization was evaluated. ESC were treated with DRSP, and proliferation, apoptosis and cell-cycle were assessed.

**Materials and Methods:** NES were cultured with DRSP (10<sup>-9</sup>-10<sup>-7</sup> M) and estradiol (10<sup>-8</sup> M). Decidualization was evaluated by productions of prolactin (PRL) and insulin growth factor binding protein 1 (IGFBP1). ESC were cultured with DRSP (10<sup>-7</sup>-10<sup>-5</sup> M). Proliferation, apoptosis and the cell-cycle were assessed by BrdU incorporation, annexin V staining, and flowcytometry, respectively.

**Results:** As for NES, eight days treatment of DRSP with estradiol induced decidualization in a time- and dose-dependent manner, confirmed by morphology and PRL and IGFBP1 secretion. (P < 0.05). As for ESC, DRSP significantly inhibited cell proliferation in a dose-dependent manner (P < 0.001) and induced apoptosis (P < 0.05), but did not affect cell cycle.

**Conclusion:** Our study firstly discovered that DRSP has similar characters with other progestin; causing decidualization in NES and inhibition in ESC. The inhibitory effects for endometriosis suggest that contraceptives containing DRSP, similar with other contraceptives, control endometriosis not only by stopping ovulation but also by inhibiting the growth of the lesion.

**Keywords:** Drospirenone, Endometriosis, Decidualization

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**EVALUATION OF ANGIOGENESIS IN EXPERIMENTAL ENDOMETRIOSIS IN WISTAR RATS TREATED WITH BEVACIZUMAB**

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**Objectives:** To evaluate the angiogenesis effect by the action of the monoclonal antibody Bevacizumab in the treatment of retrocervical endometriosis in Wistar rats.

**Design:** Study design is prospective and experimental study

**Materials and Methods:** We prepared slides with tissue of retrocervical endometriosis implants, surgically fixed, removed after testing medications. We studied 57 Wistar rats divided into three groups, leuprolide acetate, Bevacizumab and control respectively. After prepared for immunohistochemistry. For staining was selected marker angiogenesis anti-VEGF. For reading, photographs were taken.

**Results:** The mean reading by immunohistochemistry in Leuprolide group was 351.7  $\mu\text{m}^2$ , Avastin group was 73.8  $\mu\text{m}^2$  and 12.6  $\mu\text{m}^2$  in the Control group. The comparison between groups Avastin Lupron and Lupron and Control showed a reduction of endometrial implants in the group treated with Avastin ( $p < 0.001$ ). Between groups Avastin and Control the value of  $p = 0.171$ .

**Conclusion:** The treatment of bevacizumab reduced endometrial implants but it was not effective in reducing angiogenesis in Wistar rats.

**Keywords:** Endometriosis, VEGF, bevacizumab

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### DIENOGEST IS A SAFE AND EFFECTIVE TREATMENT FOR CHRONIC PELVIC PAIN ASSOCIATED TO ENDOMETRIOSIS

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**Objectives:** To assess the safety and efficacy of dienogest 2mg/day for the long-term treatment of endometriosis associated pain, and to evaluate adverse effects and improvement in quality life for long-term endometriosis treatment.

**Design:** A prospective, open-label extension study

**Materials and Methods:** Ninety three patients with chronic pelvic pain were divided into three groups: 1) suspicious of endometriosis without laparoscopic confirmation 2) confirmed laparoscopic diagnosis and immediate fertility desire 3) confirmed laparoscopic diagnosis without medical treatment after the surgery. Efficacy was assessed by changes in endometriosis-associated pelvic pain.

**Results:** Fifty three patients completed the trial. Main reasons for discontinuation were adverse effects (5), economic reasons (6), protocol deviations (4), not completing at least six months of treatment (16). Results at 6 months of treatment: Group 1 (n:11): no pain 72%, mild pain 27%; patients without adverse effects 63%; normal bleeding (9%), infrequent bleeding (27%), amenorrhea (63%). Group 2(n:26): no pain 85,7%, mild pain 14,2%; patients without adverse effects 69, 21%; normal bleeding (3, 84%), infrequent bleeding (19%), amenorrhea (73%). Group 3(n:21): no pain 80,95%, mild pain 13,80%; severe pain 4,76%; patients without adverse effects 61,90%; normal bleeding (6,52%), infrequent bleeding (13,28%), amenorrhea (80,95%)

**Conclusion:** Patients treated with dienogest showed sustained decrease in endometriosis-associated pelvic pain. Irregularities in bleeding pattern and other adverse effects were well tolerated in light of accompanying pain relief. Dienogest offers an effective and long-term option for endometriosis; and an excellent treatment to avoid recurrence and preserve fertility.

**Keywords:** Endometriosis, dienogest, pelvic-pain

## Poster - Medical treatment

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### SHOULD MEDICAL TREATMENT FOR DYSMENORRHEA IN ADOLESCENTS BE CYCLIC OR CONTINUOUS CONTRACEPTIVE PRESCRIPTION

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**Objectives:** To evaluate the efficacy of medical treatment with contraceptives to dysmenorrhea in adolescents comparing cyclic and continuous prescription.

**Design:** Longitudinal prospective study initiated at January 2013 and data will be presented until October 2013. Adolescents attended at Gynecology for Adolescents Out-clinic at Hospital Servidor Público Estadual who had more than 2 year from the menarche and presented dysmenorrhea without medical response to nonsteroids anti inflammatory were offered contraceptive treatment.

**Materials and Methods:** The choice between cyclic or continuous use was made by the adolescents and their accompanying during first consultation. Analysis of level of pain was made using a Visual Analogic Scale (VAS). Every 2 months and efficacy of the treatment were evaluated in order to obtain a better quality of life.

**Results:** Fifty-four adolescents completed 3 appointments. Mean age was 16,01 year (13– 18) comparison between group that started with cyclic or continuous prescription didn't show any difference in age ( $p=0,32$  IC: -0,40a -1,21). Difference between level of pain before treatment and after last consultation using any modality of contraceptive prescription was significant ( $p < 0,0000001$ ; IC: 5,33– 7,11). Although just 40,47% from the group using cyclic contraceptives had shown improvement at pain's level from high or moderate to mild at VAS, difference between initial (8,09) and two-month (4,57) means were statistically relevant ( $p < 0,0000001$ ; IC: 2,52– 4,52). Nevertheless, those girls were oriented to use the continuous prescription. Comparison between means (8,83- 1,25) from continuous group was also significant ( $p < 0,000001$ ; IC: 6,03– 9,13).

**Conclusion:** Any modality of prescription, cyclic or continuous, had shown good response to decrease scores of pain in adolescents with dysmenorrhea without previous improvement with nonsteroidal anti inflammatory drugs.

**Keywords:** Adolescents, dysmenorrhea, contraceptives

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**USE OF APITOXIN AS A TREATMENT OF EXPERIMENTAL RETROCERVICAL AND INTESTINAL ENDOMETRIOSIS**

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**Objectives:** To evaluate the treatment of intestinal and retrocervical Endometriosis in Wistar rats with dehydrated bee venom (apitoxin).

**Design:** prospective and experimental study with Wistar rats

**Materials and Methods:** 60 female Wistar rats were induced by retrocervical and intestinal endometriosis. After 21 days, both were divided into 3 groups for the treatment: control (n = 10), leuprolide (n = 10) and apitoxin (n = 10). After sacrifice, histological analysis were done

**Results:** The intestinal implants increased more than retrocervical after 21 days (32.1 mm<sup>2</sup> versus 27.7 mm<sup>2</sup>), but retrocervical implants were larger at 60th day in control groups (58.1 mm<sup>2</sup> versus 53.8 mm<sup>2</sup>, p=0,059). Both control groups showed increased area, while the groups treated with Leuprolide reduced the implants (retrocervical reduced 6 mm<sup>2</sup>, p=0,015 and intestinal 3.1 mm<sup>2</sup>, p=0,065). Apitoxin treated groups also showed growth, but smaller areas than the control

**Conclusion:** The two models of deep endometriosis were effective in the development of experimental endometriosis. The use of apitoxin was effective to reduce the growth of endometrial implants in intestinal and retrocervical models of experimental endometriosis

**Keywords:** Endometriosis, treatment, apitoxin

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**REDUCED PELVIC PAIN IN WOMEN WITH ENDOMETRIOSIS: EFFICACY OF DIENOGEST AFTER 6 MONTH CONTINUOUS TREATMENT**

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**Objectives:** To investigate the efficacy and safety of dienogest treatment in endometriosis cases after one year follow up. The study included women with endometriosis, who had previously completed at least 12-week of dienogest, after one year follow up.

**Design:** We have performed a prospective study.

**Materials and Methods:** From August 2012 to August 2013, 250 women with endometriosis stages I or II diagnosed by clinical examination and transvaginal ultrasound with bowel preparation enrolled the study. All women received dienogest (2 mg) and changes in pelvic pain, bleeding pattern, adverse events and ultrasound parameters were evaluated during treatment.

**Results:** All women complaint of pelvic pain (100%), dyspareunia (78%) or acyclic pain (26%) before medication. The completion rate among women who entered the open-label extension study was 95.2% (n = 238). A significant decrease in pelvic pain (evaluated on a visual analog scale) was shown during continued dienogest treatment (P < 0.001). The mean frequency and intensity of bleeding progressively decreased after 2 months of continuous medication. Twelve patients had adverse events, that led them to withdrawal study. Transvaginal ultrasound with bowel preparation was performed in the beginning of the study and after 6 months with continuously medication. Between these patients (who had at least 6 months of follow up), 57% (n= 94/164) had reduction of the endometriotic nodules or cysts in ultrasound examination.

**Conclusion:** Long-term dienogest 2 mg daily alleviates the painful symptoms of endometriosis, reduces endometriotic lesions, and improves quality of life. Dienogest also demonstrated a favorable safety and tolerability profile with low adverse effects, high rates of patient compliance, and low withdrawal rates.

**Keywords:** Dienogest, pain, endometriosis

**Poster - Medical treatment**

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**MANAGEMENT OF THORACIC ENDOMETRIOSIS: CASE SERIES AND REVIEW OF THE LITERATURE**

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**Objectives:** Thoracic endometriosis syndrome, characterized by the presence of functional endometrial tissue within the pleura, lung parenchyma or tracheobronchial system, is a rare presentation that can cause significant morbidity. The objective of our series is to present the management approach for this complex manifestation of endometriosis at our centre.

**Design:** Case series of four patients with thoracic endometriosis treated at a tertiary care clinic in Canada specializing in the management of endometriosis.

**Materials and Methods:** Our patients were treated with conservative management (GnRH agonist, letrozole) in collaboration with a thoracic surgery team.

**Results:** Due to the severity of the pulmonary symptomatology, some patients received surgical intervention by the thoracic surgery prior to their referral to our centre. Following referral and medical management, all five patients had excellent outcomes with improvement in pain as well as decreased episodes of pulmonary symptoms. Suppression was achieved with medical management without the need to undergo further thoracic surgery.

**Conclusion:** Thoracic endometriosis can successfully be managed without requiring extensive thoracic surgical intervention.

**Keywords:** Endometriosis, Thoracic, GnRH-agonist

## Poster - Medical treatment

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### ATTEMPTS TO IMPROVE PATIENT ADHERENCE TO HORMONE THERAPY AFTER ENDOMETRIOSIS SURGERY

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**Objectives:** Endometriosis management necessitates selecting pharmaceutical and surgical treatments tailored to individual patients' symptoms, age, disease history, and other factors. Particularly in young women through the sexual maturation period, it is essential to determine the optimal timing of surgery and to prevent postoperative relapse, taking into account ovarian function preservation.

**Design:** At our facility, when dealing with patients younger than age 40 with no plans for children, we generally administer postoperative hormone therapy, and have achieved a medication adherence rate of at least 90% one year after starting this therapy. Herein, we present our application of this therapy.

**Materials and Methods:** Background variables were investigated in 151 patients receiving postoperative hormone therapy between April 2013 and September 2013. According to our postoperative management policy for endometriosis patients, an ethinylestradiol (EE) 0.035 mg/norethisterone (NET) 1.0 mg combination is the first-line drug. If this preparation causes problems, treatment is switched to another drug.

**Results:** The prescriptions at the time of investigation were EE/NET, EE 0.020 mg/drospirenone (DRSP) 3.0 mg, and dienogest in 128, 12, and 11 cases, respectively. In 11 of the 12 patients receiving the EE/DRSP combination, treatment had been switched from EE/NET due to adverse reactions (nausea, edema, acne vulgaris, weight gain, depression, headache). Of the 11 patients receiving dienogest, 9 were 40 or older, and 5 had been switched from the EE/NET combination to dienogest because of adverse reactions to low-dose estrogen-progestin (LEP), lack of symptom alleviation with LEP, and elevated thrombosis risk due to age exceeding 40.

**Conclusion:** Although consensus has been reached as to the validity of long-term LEP for treating endometriosis, drop-out from this hormone therapy is frequent. In our facility, adherence to hormone therapy has been improved by using an EE/NET combination as the first-line drug and switching to other drugs depending on adverse reactions.

**Keywords:** Adherence, hormone therapy

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**THE EFFECT OF DIENOGEST (ALLURENE®) ON PELVIC PAIN AND ABNORMAL UTERINE BLEEDING IN WOMEN WITH INTESTINAL ENDOMETRIOSIS.**

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**Objectives:** To evaluate the effects of dienogest (Allurene®) on pelvic pain and uterine bleeding patterns in women with intestinal endometriosis.

**Design:** Were studied 14 patients with an average age of 36.6 years. Those patients were diagnosed with intestinal endometriosis through intestinal prepared transvaginal ultrasonography exam, without videolaparoscopy. It was ministred to them orally 2mg of dienogest (Allurene®) per day, during 180 days.

**Materials and Methods:** The clinical pelvic pain (dysmenorrhea) was measured via visual analogue scale (VAS) prior to the beginning of the treatment, and with 30, 60, 90 and 180 of medicine ministratation. The uterine bleeding patterns were also observed on the given period.

**Results:** Regarding pelvic pain, the VAS method reached an avarege of 9.2. Throughout the treatment length, with 30, 60, 90 and 180 days of treatment, the respective values were: 3.6, 2.6, 2.5 and 2.1. The bleeding patterns among the patients were 5 with abnormal bleeding (35.7%), 3 with frequent bleeding and 2 with extended bleeding.

**Conclusion:** Regarding pelvic pain, the VAS method reached an avarege of 9.2. Throughout the treatment length, with 30, 60, 90 and 180 days of treatment, the respective values were: 3.6, 2.6, 2.5 and 2.1. The bleeding patterns among the patients were 5 with abnormal bleeding (35.7%).

**Keywords:** Pelvic paim, dienogest

## Poster - Pain and pain mechanisms

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### IMAGING CENTRAL PAIN NETWORKS IN WOMEN WITH CHRONIC PELVIC PAIN

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**Objectives:** Resting state networks (RSNs) are believed to represent the brain's activity whilst not attending to an external task. We believe that the study of RSNs might lead to insights on the functionality of certain pain pathways in women with chronic pelvic pain (CPP) and identify potential novel therapeutic targets.

**Design:** A prospective cohort study using functional magnetic resonance imaging (fMRI) of the brain.

**Materials and Methods:** Women with CPP were recruited. They completed pain ratings, validated disease-relevant questionnaires and underwent fMRI brain scan (3T Siemens). Data was analysed using MELODIC (FMRI's software library (FSL)) to identify brain networks common to the subjects.

**Results:** Subjects reported ratings for non-cyclical pain (range 0-6, median 3.5), dysmenorrhea (range 0-9, median 6), dyspareunia (range 6-9, median 7) and background pain on the day of the scan (range 0-7, median 0.5). Group independent component analysis was performed on the six complete data sets obtained to date. This yielded RSNs comprising important pain processing regions. These networks included: i) brainstem, insula, and primary somatosensory cortex (S1); ii) hippocampus and inferior frontal gyrus (IFG); iii) brainstem, thalamus, and insula; iv) thalamus and primary somatosensory cortex (S1). Of note, these are all regions involved in the processing of acute painful stimuli and many have been shown to amplify pain in other chronic pain conditions. We are working to increase the cohort size.

**Conclusion:** The results suggest that fMRI is a robust tool to image brain activity relevant to endometriosis-associated pain, with the potential to identify novel therapeutic targets. Using neuromodulators to manage CPP is supported by the identification of brainstem networks, whilst networks including IFG suggest psychological therapies may also be beneficial.

**Keywords:** fMRI, brain, pain

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**ILIOINGUINAL AND ILIOHYPOGASTRIC LAPAROSCOPIC NEURECTOMIES FOR THE TREATMENT OF CHRONIC NEUROPATHIC PAIN**

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**Objectives:** To identify ilioinguinal and iliohypogastric entrapment as a cause of chronic pelvic pain and to offer a feasible laparoscopic treatment

**Design:** In this Prospective study we performed 8 ilioinguinal and iliohypogastric laparoscopic neurectomies at the level of the quadratus lumborum.

**Materials and Methods:** 8 women with chronic pelvic pain ( due to neuropathic pain) were included in this study. A laparoscopic procedure was performed aiming lysis of adhesions (at the level of quadratus lumborum) and identification and section of these nerves. Month post-operative evaluation for a period of 6 months was conducted.

**Results:** Eight women with CPP due to neuropathic pain were identified. The pain was of > 6 months in duration and interfered with daily life activities. Month post-operative evaluation for a period of 6 months was conducted. All 8 patients were treated with laparoscopic neurectomies of the ilioinguinal and iliohypogastric nerves, with completely relief of symptoms

**Conclusion:** Our technique appears to be feasible and offers good results in terms of the treatment of chronic neuropathic pain caused by ilioinguinal and iliohypogastric entrapment.

**Keywords:** Entrapment, chronic pain

## Poster - Pain and pain mechanisms

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### ESTROGEN, A CRUCIAL MEDIATOR OF THE PEPTIDERGIC AND NORADRENERGIC NERVE FIBRE IMBALANCE IN PERITONEAL ENDOMETRIOTIC LESIONS

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**Objectives:** Recently, we were able to detect a dominance of proinflammatory peptidergic nerve fibers (NF) over noradrenergic anti-inflammatory NF in peritoneal endometriotic lesions (pEL), which may explain the variety of pain symptom in endometriosis. pEL induce a chronic inflammatory response, with an increased secretion of pain mediators and estrogen.

**Design:** Many painful conditions occur more frequently in women and it is shown that estrogen has neuromodulatory effects. This study investigates the role of estrogen on the disturbed innervation in peritoneal endometriosis using an in vitro neurite-outgrowth-assay and ex vivo measurements of estrogen in the peritoneal fluid of endometriosis patients.

**Materials and Methods:** Estrogen-concentration was measured in peritoneal fluids (PF) using ELISA (n=150). Healthy peritoneum and pEL were analysed using immunofluorescence (ER $\alpha$ / $\beta$  double staining with a neuronal marker). Chicken sensory and sympathetic ganglia were treated with estrogen or PF and the neurite-outgrowth was evaluated, before used for expression analysis (qPCR) and western blotting.

**Results:** PF from endometriosis (EM)-patients contains significantly higher levels of estrogen compared to the control group (p<0.001). Both ERs are localized on EM-associated PGP9.5-immunoreactive nerve fibres. Estrogen induced a neurite outgrowth in sensory DRG, whereas, increasing concentrations of estrogen led to a significant reduction of sympathetic outgrowth compared to a treatment with medium alone (p<0.05). PF from endometriosis-patients induced a significantly stronger sensory neurite outgrowth and a reduced sympathetic sprouting when compared to the control group (p<0.001). Sensory and sympathetic ganglia treated with PF from EM-patients express significantly higher levels of ER $\alpha$  but significantly lower ER $\beta$  levels (mRNA and protein) compared to the control (p<0.001). ER $\alpha$ /ER $\beta$  ratio in sympathetic but not in sensory ganglia treated with PF from EM-patients was shifted compared to the control group.

**Conclusion:** Estrogen is elevated in the PF of endometriosis-patients, both ERs are expressed on endometriosis-associated NF, and estrogen induced a neurite outgrowth from sensory but reduced a neurite-sprouting from sympathetic ganglia, therefore, we believe that the existing imbalance between peptidergic and noradrenergic innervation and the pain symptomatology in endometriosis is estrogen-dependent.

**Keywords:** Estrogen, innervation, pain

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### VALIDATION OF POTENTIAL ASSESSMENT TOOLS FOR DIAGNOSING NEUROPATHIC PAIN IN WOMEN WITH ENDOMETRIOSIS: A PILOT STUDY

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**Objectives:** The underlying aetiology of endometriosis-associated pain is complex but it likely has nociceptive, inflammatory and neuropathic components. Diagnosing neuropathic pain (NPP) in women with chronic pelvic pain (CPP) is challenging. We aimed to determine whether a questionnaire could be effective for diagnosing NPP in women with CPP.

**Design:** Prospective cohort study of women with CPP presenting to UK hospital over 12 months. Sample size was calculated as 72, assuming expected 70% negative diagnosis (based on retrospective data) for presence of NPP and was powered for specificity of 85%+/-10% (based on validation of questionnaires in NPP outside reproductive tract).

**Materials and Methods:** Women with CPP were invited to complete the NPP questionnaires S-LANSS, painDETECT and DN4, and undergo quantitative sensory testing (QST) by a trained clinician. Following the assessments they were asked to complete a patient acceptability questionnaire. Their case records were interrogated for associated pathology.

**Results:** 41 women have been recruited to date and this represents an interim analysis of their data. 32% (13/41) had a QST suggestive of NPP. 35% (7/20) of the women with underlying endometriosis (20/41) were QST positive. The highest rates were seen in those with stage IV disease (57%) compared to those with stage I (29%). In women with no obvious associated pelvic pathology (normal laparoscopy) only 21% (9/41) were QST positive. Specificity for the S-LANSS, painDETECT and DN4 were 46%, 75% and 68% respectively, and sensitivity 62%, 57% and 31%. PainDETECT had the highest positive and negative predictive value (50 and 80% respectively). There were high levels of confidence in the questionnaires (97%) and patients found them easy to complete unaided.

**Conclusion:** This study suggests that endometriosis-associated pain frequently has a neuropathic component. The PainDETECT questionnaire could potentially enable future large-scale studies to determine its true prevalence. Ultimately, PainDETECT could also be used to facilitate early, targeted therapy with neuromodulators, reducing other unnecessary medical and surgical treatments.

**Keywords:** Neuropathic pain, assessment

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### INTERRELATIONSHIP AMONG CLINICAL SIGNS OF CENTRAL SENSITIZATION, MYOFASCIAL DYSFUNCTION, HISTORY OF ENDOMETRIOSIS, LEVATOR SPASM AND MIGRAINES IN WOMEN WITH ENDOMETRIOSIS-ASSOCIATED CHRONIC PELVIC PAIN

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**Objectives:** Clinical signs of central sensitization may portend the relationship between chronic pelvic pain (CPP) and endometriosis. We evaluated whether migraines, levator spasm, endometriosis characteristics, myofascial dysfunction (MyoDys) and abuse were associated with sensitization in the pelvic region of women with chronic pelvic pain suggesting endometriosis compared to healthy volunteers (HV).

**Design:** Prospective cohort study of CPP and current endometriosis (CPP-endo-now; n=18), CPP only (CPP-no-endo-now; n=11), and HV (n=20); those with CPP underwent surgery for diagnosis/ treatment of any endometriosis lesions. Sensitization was defined as >6 abnormal segments per side during assessment from T9-S2 for allodynia or hyperalgesia.

**Materials and Methods:** Headaches and pain were assessed by questionnaire. Levator spasm was detected on exam. Abuse was self-reported. Myofascial-trigger-points (TrP) were examined in 7 muscles per side. MyoDys was defined as having TrP in ≥4 muscles per side. Trends were assessed by Kruskal-Wallis test for trend and logistic regression modeling.

**Results:** Women with CPP, regardless of endometriosis, had high rates of sensitization (83%vs82%vs15%) compared to HV, but those with history of endometriosis most likely to be sensitized (87%vs67%vs15%; p<0.001). 61% of women with CPP-endo-now had levator spasm compared to 36% CPP-no-endo-now vs 0% HV (p<0.0001). Overall, those with migraines (p<0.001) and levator spasm (p=0.004) were more likely to have sensitization, an association that did not persist after adjusting for group. Endometriosis severity, lesion depth and abuse were not associated with sensitization. After adjusting for group, those with more severe headaches, body pain, and pelvic pain (OR=2.29, 95% CI:1.14-4.59;p=0.02) or MyoDys (OR=6.81,95%CI:1.04-44.36;p=0.045) were more likely to have sensitization. In considering any history of endometriosis instead of group, those with MyoDys were most likely to have sensitization (OR=9.41,95%CI:1.77-50.08;p=0.009).

**Conclusion:** Individual factors associated with CPP may not be associated with sensitization in women with endometriosis. However, factors considered together, especially in those with any history of endometriosis, appear to be associated with sensitization. Conceptualizing these interrelationships may be important in the treatment of women with endometriosis-associated chronic pelvic pain.

**Keywords:** Sensitization, pain, endometriosis

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### DYNAMIC WEIGHT BEARING (DWB) EMPLOYED AS A NEW CONCEPT FOR QUANTIFICATION OF PELVIC PAIN IN A PRE-CLINICAL MODEL

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**Objectives:** Chronic pelvic pain (CPP) is defined as long-lasting and severe pelvic pain persisting over 6 months. It is a major symptom of endometriosis. Pharmacological approaches addressing CPP are hampered by the fact that no specific, validated animal model for pelvic pain is available.

**Design:** In the presented study, the newly developed dynamic weight bearing system (Bioseb, France) was employed for quantification of pelvic pain in a rat model for peritonitis.

**Materials and Methods:** DWB analyses the weight distribution of an animal on the 4 paws. Han-Wistar rats were treated with rofecoxib or vehicle and received 30 min later an i.p. application of LPS. DWB was performed 5 hours after first application. Peritoneal lavage sampling followed 1 hour later (post mortem).

**Results:** DWB analysis revealed that rats treated with LPS i.p. showed 5 hours after application a significantly increased weight distribution to the front from the hind paws when compared to vehicle-treated animals. This is indicative of a relief posture associated with pelvic pain by LPS treatment. Pretreatment with the COX2 inhibitor rofecoxib abolished the development of relief posture indicating the sensitivity of the model for pelvic pain related to peritonitis. Post mortem analysis of the peritoneal fluid of the animals revealed increased PGE2 levels after LPS treatments which were significantly decreased in all rofecoxib treated groups.

**Conclusion:** Taken together, we were able to show that DWB combined with LPS-induced peritonitis may deliver a new animal model addressing pelvic pain with high construct validity (peritoneal inflammation), predictive validity (effect of COX inhibitor in relevant dose), and face validity (pain related relief posture).

**Keywords:** DWB, peritonitis, rats

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### UTERINE AXON DISTRIBUTION IN WOMEN WITH DIFFERING MENSTRUAL PAIN SYMPTOMS

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**Objectives:** Recent studies suggest that aberrant innervation is present in uteri from women with endometriosis; others suggest that abnormal patterns occur more generally in uteri from women with pain. We aim to determine whether aberrant innervation is present in myometrium and/or endometrium of women with endometriosis and varying pelvic pain symptoms.

**Design:** Full thickness uterine samples are collected from women undergoing hysterectomy for analysis of nerve fibre density, distribution and phenotype. Patients are classified based on presence/absence of endometriosis and other comorbidities (eg. uterine fibroids, adenomyosis) as well as the severity of pelvic pain symptoms, particularly dysmenorrhea.

**Materials and Methods:** Tissues are fixed (4% paraformaldehyde) and cryoprotected before freezing. Fluorescent immunostaining (16µm sections) using antibodies against pan-neuronal marker PGP9.5 and either CD31 or αSMA will be used to label axons and blood vessels or smooth muscle, respectively. The axon density and distribution patterns in different uterine regions will be examined.

**Results:** To date, full thickness hysterectomy samples have been collected from 7 women and matched clinical and symptom information collated (4 of 7 report severe dysmenorrhea). Dual immunofluorescent protocols with PGP9.5/CD31 and PGP9.5/αSMA have been developed and initial staining with hysterectomy samples illustrates a distinct axon population in the myometrium; endometrial tissues have yet to be examined. Qualitative and quantitative analysis of uterine axons is ongoing.

**Conclusion:** Ongoing studies will provide detailed information about the distribution of axons in non-pregnant uterine tissues in women with varying pathologies and pelvic pain symptoms. Future analyses examining markers of nociceptive axons in uterine tissues are planned.

**Keywords:** Axons, pelvic pain

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### PELVIC FLOOR TENDERNESS IN CHRONIC PELVIC PAIN: PREVALENCE AND PREDICTORS

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**Objectives:** Chronic pelvic pain (CPP) affects ~15% of women. Musculoskeletal causes of CPP can manifest as pelvic floor tenderness. We hypothesize that pelvic floor tenderness is common in CPP.

**Design:** Retrospective review of 100 consecutive cases of women with CPP seen at a tertiary referral centre.

**Materials and Methods:** Every patient was examined for pelvic floor tenderness by palpation of the levator ani on pelvic exam: tenderness was coded as present or absent. Logistic regression was used to identify variables on history that were independently associated with pelvic floor tenderness.

**Results:** Average age was 32.8 +/- 8.8 years (+/- SD), average BMI was 26.3 +/- 7.0, and 43% were parous. About half of cases (46%) had endometriosis. Pelvic floor tenderness was present in 38 cases (38%). Pelvic floor tenderness was independently associated with non-dysmenorrhea CPP ( $p = 0.05$ ,  $b = 1.39$ ) (defined as any chronic pelvic pain other than dysmenorrhea) and with superficial dyspareunia ( $p = 0.017$ , 1.29). Pelvic floor tenderness was not associated with age, parity, BMI, dysmenorrhea, deep dyspareunia, bowel symptoms, or bladder symptoms, and was similarly frequent in women with endometriosis (41%; 19/46) and without endometriosis (35%; 19/54) ( $p = 0.54$ ).

**Conclusion:** Pelvic floor tenderness is common in women with CPP. A tender pelvic floor may play a role in non-dysmenorrhea CPP and superficial dyspareunia. Pelvic floor tenderness can be present in women with endometriosis as well as women without endometriosis presenting with CPP.

**Keywords:** Pelvic pain endometriosis

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### MULTIPLE VISCERAL SYMPTOMS IN ENDOMETRIOSIS

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**Objectives:** Animal studies suggest a causal link between endometriosis and abdominal organ dysfunction through viscera-visceral autonomous reflexes. In this study we compared the occurrence of symptoms related to abdominal organs in endometriosis patients and a reference group of women not suffering from the disease.

**Design:** An electronic questionnaire, developed to collect information on pain and other endometriosis related symptoms, was completed by 610 patients with diagnosed endometriosis and 751 reference women. Respondents were recruited via the Danish Endometriosis Association, the Endometriosis Center at Aarhus University, a major Danish union and Facebook.

**Materials and Methods:** Percentages were reported for all data. Principal component analysis was used to find underlying structures of correlations among variables, and Chronbach's alfa reliability analysis was used to demonstrate internal consistency of each scale. The level of statistical significance was set at  $p < 0,025$  in all analyses.

**Results:** Principal component analysis indicated the occurrence of a specific abdominal visceral symptom-complex in endometriosis patients, when compared to reference women. This "visceral syndrome" consisted of 7 symptoms; "abdominal pain with no relation to menstruation", "pain during urination", "pain during defecation", "constipation or diarrhea", "irregular bleeding", "nausea or vomiting" and "feeling tired/lack of energy", with a Chronbach's alfa value  $\alpha = 0.85$ . Women with endometriosis suffered more often than reference women between 5-7 symptoms from the visceral syndrome (22.7 % vs. 2.7 %). Even when analysis was restricted to include only women with pain, endometriosis patients suffered more than reference women with pain due to other causes from 5-7 symptoms from the visceral syndrome (22.7 % vs. 3.2 %).

**Conclusion:** These data indicate that a significant number of endometriosis patients seem to suffer from a specific symptom correlation, which is uncommon in women without the disease. Together with previous studies, this may suggest the occurrence of an abdominal visceral syndrome in endometriosis.

**Keywords:** Visceral symptoms; pain

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**SIMPLIFIED TECHNIQUE INJECTING BOTULINUM TOXIN A TO OBTURATOR INTERNUS USING NERVE STIMULATION AND ULTRASOUND TECHNIQUE FOR MANAGEMENT OF PELVIC PAIN**

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**Objectives:** To describe a simplified technique for trans-obturator foramen injection of botulinum toxin injection technique for management of stabbing pains due to obturator internus spasm in women with chronic pelvic pain

**Design:** Identification of technical difficulties encountered with current injection techniques. These include inability to identify muscle twitch using tactile assessment techniques, difficulty with muscle isolation using the nerve stimulator in patients with high body mass index and incomplete muscle injection with nerve stimulation alone.

**Materials and Methods:** Description of equipment used for nerve stimulator localisation of obturator internus with video demonstration Description of equipment used for concurrent ultrasound visualisation of obturator internus with video demonstration

**Results:** The technique demonstrated uses nerve stimulation at 2Hz, 1mA of the obturator internus muscle via the obturator foramen using equipment available in most operating theatre suites. Such stimulation elicits an external visualised needle twitch once the muscle is entered. Concurrent ultrasound visualisation of the muscles of the pelvic side wall using a hand held linear array ultrasound probe over the symphysis pubis allows visualisation of the muscle twitch produced and the ability to ensure that all muscle bundles are treated.

**Conclusion:** The technique of concurrent nerve stimulation and ultrasound to localise obturator internus, simplifies the procedure and is within the capability of general gynaecologists.

**Keywords:** Botulinum toxin pain

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### MALADAPTIVE NOCICEPTION CONTRIBUTES TO PAIN IN ENDOMETRIOSIS

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**Objectives:** To assess peripheral and central nociceptive system changes in women with endometriosis. Endometriosis-associated chronic pain symptoms are dynamic and do not correlate with anatomical disease severity. How pain persists may be related to sensory innervation of lesions and eutopic endometrium. Innervation implies peripheral nociception and persistent pain signals central nociception.

**Design:** In a case-control study of reproductive-aged women, Quantitative Sensory Testing (QST) was used to measure how nociceptive stimuli are perceived in women with persistent endometriosis-associated pain, compared to pain-free controls. QST activates the nociceptive system by the application of defined stimuli to cutaneous sites in a controlled laboratory setting.

**Materials and Methods:** Nineteen confirmed-endometriosis and 20 control-women rated the intensity of a single pinprick stimulus and of a series of 10 pinprick stimuli, at one second intervals; scored as 0-no pain to 100-worst possible pain. Application sites included the dorsum hand (C7), abdomen (T11) and back (L4). Pain intensity scores were analysed.

**Results:** Preliminary findings suggested that women with endometriosis experienced changes in pain sensitivity in regions close to the confirmed pathology: low abdomen and low back. Stimuli applied to the low back of women with endometriosis elicited higher pain intensity scores that also correlated with higher ratings of pain with intercourse ( $r=0.63$ ,  $p=0.006$ ), compared with controls with no persistent pain. Additionally, in women with endometriosis, greater back sensitivity to stimuli correlated with greater abdominal sensitivity ( $r=0.58$ ,  $p=0.01$ ) which, in turn, correlated with greater hand sensitivity ( $r=0.54$ ,  $p=0.01$ ). Greater hand sensitivity suggests changes in pain processing at regions distant to the confirmed pathology. Together, these data suggest widespread pain sensitivity changes occur in women with painful endometriosis.

**Conclusion:** QST explores the processing of nociceptive information peripherally and centrally. These preliminary results suggest persistent endometriosis-associated pain involves maladaptive nociception: altered activation threshold, increased firing and decreased nociceptive inhibition; leading to sensitisation. Sensitisation involves enlarged nociceptive receptive fields, enhanced response to sensory inputs and is a pathway to chronic pain.

**Keywords:** pain, nociception, QST

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### FREQUENCY OF DYSMENORRHEA IN RANDOM QUESTIONNAIRES USED AT SPECIALIZED GYNECOLOGICAL APPROACH FOR ADOLESCENTS

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**Objectives:** To observe the frequency of dysmenorrhea among adolescent girls who attended Specialized Gynecologic Consultations and their perception about the sense of normality of their own menstrual cycles.

**Design:** Transversal study which data has been collected since February 2012 and presenting data until October 2013. Monthly, at Hospital Servidor Público Estadual out-patient clinic, is presented a lecture for adolescent girls by physicians who take part at Gynecology for Adolescents Treatment.

**Materials and Methods:** Before the lecture a questionnaire was proposed to search for bleeding and pain characteristics of menstrual cycle and the adolescent's opinion if the cycle was "normal". It was established a protocol and girls with important pain were referred to another specialized clinic: "Adolescent with cramps" to receive treatment.

**Results:** From a total of 135 adolescents, mean of age was 14,74 years and mean of menarche was 11,65 years. Although only 18,5% pointed "cramps" as the symptom that motivated the search for gynecological care, dysmenorrhea had 84,4% frequency at the survey. They had dysmenorrhea for 27,58 month in average, 58,9% had pain since their first cycles and 75,8% at their first year after menarche. Seventy-three percent missed some home or school activities due to the pain in average of 2,48 days. Nevertheless, 59,4% recorded their menstrual cycle as "normal", and when excluded those girls who complaint of menstrual irregularity as the source of the anomaly of the cycle, the frequency for "normal cycle" was 70,3%, despite of the pain.

**Conclusion:** While dysmenorrhea shows a high frequency among adolescents and presents itself early in their reproductive years. Even disrupting home and school activities, few girls perceive the pain as a symptom or something out of the ordinary or expected in their lives.

**Keywords:** Adolescents, dysmenorrhea, pelvicpain

## Poster - Pain and pain mechanisms

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### ABDOMINAL WALL PAIN IN CHRONIC PELVIC PAIN: PREVALENCE AND PREDICTORS

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**Objectives:** Chronic pelvic pain (CPP) affects ~15% of women. One musculoskeletal cause of CPP is abdominal wall pain (AWP) (e.g. myofascial trigger points). We hypothesize that AWP is common in CPP and may be associated with other causes of CPP.

**Design:** Retrospective review of 100 consecutive cases of women with CPP seen at a tertiary referral centre.

**Materials and Methods:** AWP was diagnosed by positive Carnett's test (abdominal tenderness unchanged or worse with tensing of abdominal wall): AWP was coded as present or absent. Logistic regression was used to identify variables on history that were independently associated with AWP.

**Results:** Average age was 32.8 +/- 8.8 years (+/- SD), average BMI 26.3 +/- 7.0, and 43% were parous. About half of cases (46%) had endometriosis. AWP was present in 56 cases (56%). AWP was independently associated with non-dysmenorrhea CPP ( $p = 0.004$ ,  $b = 1.88$ ) (defined as any chronic pelvic pain other than dysmenorrhea) and with deep dyspareunia ( $p = 0.04$ ,  $b = 1.54$ ). AWP was not associated with age, parity, BMI, dysmenorrhea, superficial dyspareunia, bowel or bladder symptoms, and was similarly frequent in women with endometriosis (61%; 28/46) and without endometriosis (52%; 28/54) ( $p = 0.42$ ). On exam, AWP was found to be associated with pelvic floor tenderness ( $p = 0.003$ ).

**Conclusion:** Abdominal wall pain (AWP) is common in women with CPP, and may be involved in the etiology of non-dysmenorrhea CPP and deep dyspareunia. AWP can be present in women with endometriosis as well as women without endometriosis. AWP and pelvic floor tenderness co-exist, suggesting shared or related etiologies.

**Keywords:** Chronic Pelvic Pain

## Poster - Pain and pain mechanisms

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### A MULTIDIMENSIONAL PAIN SCALE TO EVALUATE CHRONIC PELVIC PAIN

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**Objectives:** Compare the Multidimensional Pain Scale (MPS) assessment of pain and quality of life with the Visual Analogue Scale (VAS).

**Design:** Cross sectional study comparing two scales for the evaluation of pain at the pelvic pain clinic.

**Materials and Methods:** A total of 37 patients with pelvic pain were evaluated and filled up the VAS and MPS. Data analysis was performed using Spearman coefficient (r), level of significance (p), confidence interval (CI), coefficient of determination (r<sup>2</sup>) and regression analysis.

**Results:** The results showed a strong, statistically significant correlation between the two scales (0.7599) (p < 0.0001). For the same score on the VAS, up to 5 different values were found using the MPS, meaning that in addition to quantifying the pain, it was also possible, with the MPS, to measure the interaction of pain with the patient's quality of life.

**Conclusion:** The MPS may be a useful tool to quantify pain while it is also sensitive for improvements or deteriorations in the life quality of the patient. These features may allow a simpler and more holistic treatment of pain.

**Keywords:** Pain score multidimensional

## Poster - Pain and pain mechanisms

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### SEXUAL INTERCOURSE AND ENDOMETRIOSIS RELATED PAIN IN A SELECTED GROUP OF PATIENTS

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**Objectives:** To describe, in a limited number of endometriosis patients, independently of the severity of the disease, the incidence and magnitude of SIP.

**Design:** Brief electronic survey designed by us, sent by email using a Monkey Survey NR platform, distributed among a selected group of patients treated by laparoscopic surgery, contacted at three different sites (Neuquén, San Isidro, and the City of Buenos Aires) while in treatment with oral contraceptives or progestagens.

**Materials and Methods:** A total of 33 emails were sent and 21 (63.33%) answers were collected in a self-allowed week's response time limit. The 21 completed surveys were analyzed using the software provided by Monkey Survey NR paid service.

**Results:** Twenty-one commented on SIP (in the last three months); of those sexually active (90,48%), 4,75% always have SIP; 28,57% frequent; 28,57% occasionally; 14,29% never; 9,52% did not had sexual intercourse in this time limit; 4,76% preferred no to answer; 46,67% with SIP have had to interrupt sexual intercourse sometimes . Surprisingly, 58,82% of the investigated population has avoided sexual intercourse due to SIP sometimes. For 55,56% pain had no relation with menstruation; for 11,11% SIP was with menstruation; 22,22% before menses; 11,11%, post menstruation and 11,11% at ovulation time. In a one to ten score, 6,25% had severe SIP, and, 6.25% had no pain. A scale of 3 was indicated by 18, 75% ; the rest, scores of 6, 25% and 12, 50%.

**Conclusion:** In a descriptive study of a limited population, no statistically significant conclusions can be derived. Interestingly, only 2 of 3 patients answered about their sexuality, and just a few had severe SIP. The fact that 58,82% had sometimes refused sexual intercourse for SIP, outstands the magnitude this issue.

**Keywords:** Sexual intercourse pain

## Poster - Pain and pain mechanisms

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### ANXIETY AND DEPRESSION IN PATIENTS WITH CHRONIC PELVIC PAIN

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**Objectives:** To evaluate anxiety and depression in chronic pelvic pain patients.

**Design:** This is a cross sectional study conducted with 26 patients with chronic pelvic pain attending a chronic pain center during 2013.

**Materials and Methods:** The Hospital Anxiety and Depression Scale (HADS) was used to identify the presence of anxiety and depression. Total scores equal or higher than 8 or 9 indicate presence of anxiety and depression respectively. Clinical information was taken from patients file. Data was analyzed using descriptive statistics.

**Results:** The mean age of the participants was 39 years old. The majority of patients were female (23 = 88.5%) and had endometriosis confirmed by Laparoscopy. Pain intensity mean was 5.6 (SD=2.5) with scores varying from 1 to 10 (VNS), pain duration varied from 3 months to 19 years ( $\bar{x}$ = 3.3 years, SD=4.4). Sixty five percent of the participants (17) scored positive for anxiety and 27% (9 patients) had scores indicating depression. Around 34% (9 participants) had positive scores for both anxiety and depression. Being positive for anxiety or depression was not associated with pain intensity (chi square=3.4 and chi square= 3.5 p=0.17 respectively). Time of onset of the disease was also not associated with anxiety (chi square=2.5 p=0.28) or depression (chi square=0.5 p=0.76).

**Conclusion:** There is a large amount of evidence suggesting that depression and anxiety are common in pain patients and that may contribute to pain and disability. Therefore it is important to treat both physical and mental conditions of these patients. Further studies with large samples should investigate better these relationships

**Keywords:** Endometriosis, anxiety, depression

Poster - Pathogenesis / aetiology

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**INHIBITION OF HYPOXIA-INDUCIBLE FACTOR-1A SUPPRESSES ENDOMETRIOSIS-ASSOCIATED ANGIOGENESIS AND GROWTH OF LESION IN A MOUSE MODEL**

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**Objectives:** Current therapeutic success in endometriosis remains unsatisfactory due to the limited insight on the mechanisms. With angiogenesis playing an essential role toward this, it imposed potential anti-angiogenesis therapy. VEGF is mediated through HIF under hypoxic condition. PX-478, an HIF-1 $\alpha$  inhibitor, may be effective in suppressing angiogenesis, and ultimately lesion growth.

**Design:** Experimental endometriosis in mice and in vivo oxidative stress and angiogenesis monitoring.

**Materials and Methods:** Experimental endometriosis model was established by subcutaneously implanting homologous mouse endometrium fragments. These mice were then treated PX-478 in 0.08mg/kg, i.p., every other day for 3 weeks. During intervention, the lesions were assessed and collected at different time-points for hypoxia and angiogenesis studies.

**Results:** We demonstrate a transient oxidative stress surge in transplanted endometriosis-like lesions with up-regulation of HIF-1 $\alpha$ , followed by dynamic increased expression of VEGF. With the systemic intervention of PX-478, it suppressed the downstream expression of HIF-1 $\alpha$  targeted genes, such as VEGF, CD31, CD34 and vWF. PX-478-treated group showed a significant decreased on vessel development and inhibited the lesion growth. Toward the safety, mice treated with PX-478 did not showed any sign of distress on the animal weight or any vascular changes toward the reproductive organs..

**Conclusion:** Our study showed that PX-478 inhibits HIF-1 $\alpha$  expression and angiogenesis in endometriosis, which ultimately suppress lesion growth. This suggested that HIF-1 $\alpha$  inhibition during the development of endometriosis may be a potential target for systemic treatment in the future.

**Keywords:** Endometriosis, Angiogenesis, HIF-1 $\alpha$

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**EFFECT OF IRON OVERLOAD ON NUCLEAR FACTOR-KAPPAB (NF-KB) PATHWAY ACTIVATION IN ENDOMETRIAL STROMAL CELLS (ESC)**

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**Objectives:** To evaluate if iron overload induce activation of the NF-κB pathway in ESC as a mechanism associated to endometriosis inflammatory response. To assess intercellular adhesion molecule (ICAM)-1 expression and soluble ICAM-1 (sICAM-1) secretion as a proinflammatory mediator regulated by iron overload-modulated NF-κB activation in ESC.

**Design:** 12 biopsies of proliferative endometrium were obtained from healthy women. ESC were isolated and incubated with 50 μM FeSO<sub>4</sub> to evaluate NF-κB activation, ICAM-1 expression and sICAM-1 secretion. NF-κB inhibitory experiments were performed by incubating ESC with the IKKβ inhibitor [5-(p-fluorophenyl)-2-ureido] thiophene-3-carboxamide (TPCA-1) previous to iron stimulation.

**Materials and Methods:** NF-κB activation was assessed by p65/DNA-binding activity immunodetection assay using nuclear protein extracts from ESC. Cytoplasmic protein extracts from ESC were used to evaluate IκBα and ICAM-1 expression by Western blot analysis. ESC sICAM-1 secretion was measured by ELISA using conditioned medium from ESC cultures.

**Results:** Iron overload increased p65/DNA binding activity in ESC after 30 minutes incubation as compared to basal condition (p<0.01), while p65/DNA binding was reduced in ESC after 6 and 24h iron overload incubation (p<0.01). Cytoplasmic ESC IκBα expression decreased at 30 minutes, 2, 6 and 24h iron overload incubation versus no iron overload condition (p<0.01). ESC ICAM-1 expression and sICAM-1 secretion were higher after 24h iron overload treatment than no iron treatment for 24h (p<0.05). Preincubation with TPCA-1 prevented the increase of p65/DNA binding activity and IκBα degradation after 30 minutes iron overload stimulus in ESC.

**Conclusion:** These results suggest a role of iron overload inducing a proendometriotic behavior in healthy ESC, involving the activation of the NF-κB pathway and stimulating the inflammatory response of these cells. Iron overload could promote IKKβ activity in the NF-κB pathway.

**Keywords:** NF-κB, iron, ICAM-1

## Poster - Pathogenesis / aetiology

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### GALECTIN-1 PLAYS A PIVOTAL ROLE IN ENDOMETRIOSIS BY PROMOTING THE VASCULAR NETWORK DEVELOPMENT IN ENDOMETRIOTIC LESIONS

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**Objectives:** Galectin-1 (Gal-1) is an endogenous lectin that plays an essential role as immunomodulatory and proangiogenic factor in cancer. However it has not been reported the involvement of Gal-1 in endometriosis pathophysiology. Thus, our main goal was to study the role of Gal-1 in growth and vascular development of endometriotic lesions.

**Design:** Endometriotic lesions were surgically induced by autologous transplantation of endometrial tissue to bowel mesentery of wild-type or Gal-1 knock-out mice for WT and KO groups respectively, by heterologous transplantation of endometrial tissue from Gal-1 knock-out to bowel mesentery of wild-type mice for hWT group, and the opposite for hKO group.

**Materials and Methods:** The number and size of endometriotic lesions were evaluated in WT, KO, hWT and hKO groups in the post-surgical day 28. Gal-1 expression and the relative vascularized area were assessed by immunohistochemistry in lesions and the concentrations of proangiogenic factors were measured in peritoneal fluid by ELISA, in all groups.

**Results:** The histological expression of Gal-1 was restricted to stromal compartment of the endometriotic lesions. The number of developed lesions decreased only in KO mice compared to WT and hKO (P=0.001). However, the lesions size was significantly reduced in KO, hWT and hKO compared to WT, by 72.6%, 78.3% and 59.7% respectively (P<0.0001). The relative vascularized area, immunostained for Von Willebrand Factor, was significantly lower in KO, hWT and hKO than WT, by 63.5%, 38.0% and 43.5% respectively (P<0.0005). Strikingly, neither the concentration of Vascular Endothelial Growth Factor in peritoneal fluid, nor the vascular expression of its type-2 receptor in endometriotic lesions showed significant differences among groups. Besides, no differences were found for the concentration of the proangiogenic factor keratinocytes-derived CXCL12 in peritoneal fluid among groups.

**Conclusion:** We demonstrated that Gal-1 exerts a pivotal proangiogenic function in vascular network development of endometriotic lesions, being this process crucial for the lesions growth and pathology progression. The possibility to identify key mediator factors involved in endometriosis pathophysiology, allow us to suggest putative therapeutic approaches to successfully treat this disease.

**Keywords:** Galectin-1, angiogenesis, pathophysiology

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**DYSREGULATION OF AUTOPHAGY INDUCTION BY ABERRANT MTOR ACTIVITY IS ASSOCIATED WITH ABNORMAL APOPTOSIS IN OVARIAN ENDOMETRIOTIC CYST**

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**Objectives:** To evaluate whether dysregulation of autophagy is mediated by aberrant mammalian target of rapamycin (mTOR) activity, a major negative regulator of autophagy, in ovarian endometriotic cyst and whether it is associated with abnormal apoptosis of endometriotic cells.

**Design:** Endometrial tissues were obtained from normal endometrium and ovarian endometriotic cysts according to menstrual cycles. Normal endometrial stromal cells (NESCs) and endometriotic cyst stromal cells (ECSCs) were cultured with/without estrogen and progesterone to mimic physiologic hormonal changes. Additionally, ECSCs were treated with rapamycin (mTOR inhibitor) with/without 3-methyladenine (3-MA, autophagy inhibitor).

**Materials and Methods:** Microtubule-associated protein light chain 3-II (LC3-II) expression and p70S6 kinase (p70S6K) phosphorylation were measured to evaluate autophagy induction and mTOR activity, respectively. Autophagy also was confirmed by the observation of autophagosomes under transmission-electron microscopy. And, apoptosis examined by and cleaved caspase-3 expression and flow cytometry of Annexin-V/propidium iodide staining.

**Results:** Endometrial cell autophagy induction was increased by mTOR inhibition as the menstrual cycle progresses in normal endometrium, and that it is correlated with apoptosis. However, in endometriotic tissue, autophagy, mTOR activity and apoptosis were constant throughout the menstrual cycle, suggesting that a constant level of autophagy is maintained by disinhibition of mTOR activity during the menstrual cycle in endometriotic tissue and is related to decreased apoptosis. Indeed, compared with normal endometrium, increased mTOR activity during the secretory phase in endometriotic tissues inhibited autophagy and apoptosis induction. In addition, although rapamycin treatment induced autophagy and led to apoptosis promotion in ECSCs, the pro-apoptotic effect of rapamycin was reversed by the addition of 3-MA, suggesting that mTOR inhibition promotes endometriotic cell apoptosis via autophagy induction.

**Conclusion:** Endometrial cell autophagy is suppressed by disinhibition of mTOR activity during the menstrual cycle in ovarian endometriotic cysts, which results in decreased apoptosis.

**Keywords:** Endometriosis, Autophagy, mTOR

## Poster - Pathogenesis / aetiology

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### MICRORNA MIR-145 - A POTENTIAL DIAGNOSTIC MARKER FUNCTIONALLY ASSOCIATED WITH PROLIFERATION, INVASION AND STEMNESS IN ENDOMETRIOSIS

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**Objectives:** microRNA expression is dysregulated in endometriosis suggesting a potential as diagnostic markers and therapeutic targets. Our objective was to study the function of miR-145 and to identify its target genes in an in vitro endometriosis model. Furthermore, we evaluated its potential diagnostic value as a noninvasive serum marker for endometriosis.

**Design:** In vitro study on an endometriotic cell line and primary endometriotic stroma cells. Diagnostic study on sera of patients and controls with laparoscopically confirmed (absence of) endometriosis.

**Materials and Methods:** Cells were transiently transfected with miR-145 precursors or inhibitors and analyzed by MTT and Matrigel invasion assay, flow cytometry, qPCR and Western blotting. Serum of 44 patients with endometriosis and 41 controls was analyzed by qPCR.

**Results:** miR-145 overexpression inhibited cell proliferation and induced down-regulation of FASCIN-1, SOX2, and MSI2. In 12Z cells, miR-145 upregulation increased Matrigel invasiveness and reduced side population and aldehyde dehydrogenase-1 activity. Additional downregulated targets in 12Z cells included OCT4, KLF4, PODXL, JAM-A, and SERPINE1/PAI-1. ACTG2 and TAGLN were up-regulated upon pre-miR-145 transfection. JAM-A, FASCIN-1, and PAI-I down-regulation in 12Z cells were confirmed by Western blotting. miR-145 was significantly downregulated in the serum of endometriosis patients ( $p < 0.05$ ).

**Conclusion:** miR-145 inhibits endometriotic cell proliferation, invasiveness, and stemness by targeting multiple pluripotency factors, cytoskeletal elements, and protease inhibitors. Its expression in serum is altered in endometriosis, harboring potential both as a noninvasive diagnostic marker and as a therapeutic target.

**Keywords:** microRNA, diagnosis, stemness

## Poster - Pathogenesis / aetiology

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### PREGNANCY AFFECTS MORPHOLOGY, PROLIFERATION AND ANGIOGENESIS OF DEVELOPING ENDOMETRIOTIC LESIONS

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**Objectives:** The aim of the study was to assess the effect of pregnancy on histology, cell proliferation and angiogenesis of endometriosis lesions in a mouse model of surgically-induced peritoneal endometriosis.

**Design:** This was a cross sectional – control versus treatment study in a mouse model of endometriosis. Thirty-one female C57Bl6 mice were mated and became pregnant (P) and 26 females were not mated (NP) and served as control.

**Materials and Methods:** Intraperitoneal endometriotic lesions were surgically induced in C57Bl6 mice which were subsequently mated (pregnant (P)) or not (non pregnant (NP)). P and NP mice were sacrificed at day E15.5 of the pregnancy of P mice. Harvested lesions were weighted and analysed by histology, immunohistology, flow cytometry and qRT-PCR.

**Results:** Pregnancy decreased endometriotic cysts' size (1301 vs 188  $\mu$ m ;  $p < 0.0001$ ). Pregnancy increased cell proliferation in both stromal (S) and glandular (G) tissue as shown by the increase in Ki 67-positive cells (S : 3.2 vs 8.7 % ;  $p < 0.01$ / G : 3.8 vs 18.9 % ;  $p < 0.001$ ). Pregnancy increased angiogenesis in endometriosis as indicated by an increase in CD-31 microvessel density (MVD) (2.2 vs 5 % ;  $p < 0.05$ ) and in LYVE-1 MVD (0.4 vs 0.9 % ;  $p < 0.05$ ) ; an increased number of LYVE1 positive cells evaluated by FACS (5.7% vs 14.3 % ;  $p < 0.05$ ) and a rise of VEGFR-2, -3 and -a RNA expression shown by qRT-PCR ( $p < 0.05$ ).

**Conclusion:** Taken together, these experimental findings suggest that pregnancy modifies endometriotic lesions' morphology with a reduction of cysts' size and an increase in proliferation and angiogenesis. Theses challenging results provide new pieces in the understanding of endometriosis pathophysiology and raise the issue of the correlation between lesion's architecture and symptomatology.

**Keywords:** Endometriosis, pregnancy, angiogenesis

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**MIS-EXPRESSION OF MIR451 AND TARGET TRANSCRIPT MACROPHAGE MIGRATION INHIBITORY FACTOR IN ENDOMETRIOTIC IMPLANT TISSUE FROM WOMEN WITH SEVERE ENDOMETRIOSIS**

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**Objectives:** Macrophage migration inhibitory factor (MIF) is mis-expressed in endometriotic tissue but the mechanism for this is uncertain. The objective of the present study was to examine the pattern of MIF mRNA and protein expression in endometriotic tissue with that of miR451; a microRNA which regulates MIF expression.

**Design:** Retrospective study using qRT-PCR, Western analysis and 3'UTR reporter constructs to assess the expression and function of miR451 and MIF in endometrium and endometriosis specimens.

**Materials and Methods:** Endometriotic implant tissue and corresponding eutopic endometrial specimens were obtained from women with severe endometriosis (N=8). MIF mRNA and protein expression were evaluated by qRT-PCR and Western blot analysis, respectively, while miR451 expression was determined by qRT-PCR. miR451 regulation of MIF expression was validated using 3'UTR reporter construct assays.

**Results:** MIF mRNA was expressed in both eutopic and ectopic endometrial tissue but exhibited no significant difference in the level of expression between tissues. In contrast, MIF protein levels were significantly reduced in endometriotic implant tissue compared to corresponding eutopic endometrium. MIF protein levels correlated with miR451 levels of expression in endometriotic implant tissue. There were no significant differences in expression of MIF (mRNA or protein) and miR451 expression based upon stage of menstrual cycle. Transfection of a human endometrial epithelial cell line with luciferase reporter constructs containing the wild-type miR451 3'UTR seed sequence for MIF confirmed that miR451 binds the 3'UTR to regulate transcript expression.

**Conclusion:** MIF mRNA and protein expression are reduced in endometriotic implant tissue compared to eutopic endometrium. miR451 expression levels were correlated with MIF protein expression suggesting that miR451 may regulate post-transcriptional MIF expression. An imbalance in the normal miR451- MIF regulatory pathway may contribute to the pathogenesis of endometriosis.

**Keywords:** Endometriosis, miR451, MIF

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**METABOLIZING ENZYMES THAT ARE RESPONSIBLE FOR THE OXIDATIVE METABOLISM OF ESTROGENS ARE INCREASED IN OVARIAN/PERITONEAL ENDOMETRIOTIC LESIONS**

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**Objectives:** Local estrogen metabolism seems to influence the progression of endometriosis. The purpose of the present study was to investigate the expression of estrogen-metabolizing enzymes responsible for oxidative metabolism (cytochrome P450 (CYP) 1B1, 1A1, and 3A4) of estrogens in eutopic and ectopic endometrium of women with or without endometriosis.

**Design:** Cross-sectional study with premenopausal women that were not using any form of hormonal treatment, and were classified according to the cycle phase: secretory phase of the menstrual cycle (progesterone >1ng/ml and days 15 - 28 of the cycle) and follicular phase (progesterone <1ng/ml and days 1 -14 of the cycle).

**Materials and Methods:** Endometrial tissue was collected from women that underwent laparoscopic surgery for indications other than endometriosis (control, n=13) or for removal of endometriotic lesions (peritoneal/ovarian and deep endometriosis, n=78). The mRNA and protein expression of the oxidative enzymes was evaluated by real time PCR and Western Blot, respectively.

**Results:** Our results indicated that mRNA and protein expression of elected CYPs did not change significantly between endometrium of women with endometriosis compared to controls (P>0.05). Notably, CYPs were significantly increased in the ovarian/peritoneal lesions ectopic endometrium of women with endometriosis when compared to eutopic or healthy endometrium. There was an approximately 6 fold increase in CYP1A1 (P=0.002) in the ovarian/peritoneal lesions in the follicular phase, whereas only a ~2 fold increase was detected in the secretory phase. Expression of CYP1B1 and CYP3A4 in ovarian/peritoneal was similarly regulated according to the menstrual cycle, although such increase was not observed in deep-infiltrating lesions. A significant reduction of CYP1A1 protein expression (P=0.04), but not of CYP1A1 and CYP1B1 (P<0.05), was overall detected in the secretory phase.

**Conclusion:** Such altered expression in ovarian/peritoneal endometriotic lesions might signify an estrogen-induced expression of CYPs in endometriotic lesions, possibly to try to compensate increased local estrogen concentration. An enhanced expression of those enzymes may contribute to milieu with estrogen metabolites that favors proliferation and endometriotic implants installation. Thanks to FAPESP (2010/02412-6)

**Keywords:** estrogen metabolism, CYP

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### INCREASED LEVELS OF TGF-B IN THE PERITONEUM OF WOMEN WITH ENDOMETRIOSIS INDUCES EMT WITHIN THE PERITONEAL MESOTHELIUM THAT MAY FACILITATE THE DEVELOPMENT OF LESIONS

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**Objectives:** TGF- $\beta$  is increased in the peritoneal fluid of women with endometriosis and is known to induce epithelial-mesenchymal transition (EMT) during fibrosis and tumorigenesis. Our aim was to determine if TGF- $\beta$  induced EMT within peritoneal mesothelial cells and examine the effects this may have on the development of endometriotic lesions.

**Design:** Ex vivo analysis of peritoneal biopsies collected from women with and without endometriosis (n=16). In vitro analysis of the effects of TGF- $\beta$ 1 on human primary peritoneal mesothelial cells (PMC), and mesothelial cell line (MeT-5A) (n=3-6).

**Materials and Methods:** Markers of EMT were localized in peritoneal biopsies by immunohistochemistry. Induction of EMT by TGF- $\beta$ 1 in PMC and MeT-5A cells in vitro was assessed by PCR-array, qRT-PCR and immunohistochemistry. The effect of EMT was assessed by morphology and migration and invasion assays.

**Results:** Immunolocalisation of pSmad2/3 to the PMC of peritoneal biopsies confirmed peritoneal TGF- $\beta$  pathway activation. Markers of fibrotic and neoplastic EMT (N-cadherin, smooth muscle actin, collagen, fibronectin, snail-1 and Forkhead box C2) were expressed in the peritoneal mesothelial cells. PCR array analysis of PMC exposed to TGF- $\beta$ 1 revealed significant increases in genes associated with EMT including; E-cadherin (2.2-fold), N-cadherin (1.9-fold), snail-1 (5.1-fold), forkhead box C2 (21.4-fold) collagen 5A2 (1.7-fold) and MMP3 (2.1-fold). These results were confirmed by qRT-PCR and immunostaining of PMC and MeT-5A cells. TGF- $\beta$ 1 induced changes in cell morphology and cytoskeletal structure of PMC and MeT-5A cells. MeT-5A cells exposed to TGF- $\beta$ 1, demonstrated increased migration (p<0.001) and invasion (p<0.05).

**Conclusion:** Our data suggests that TGF- $\beta$ 1 is increased in the peritoneal fluid of women with endometriosis and that this may induce EMT processes within the pelvic mesothelial cells, increasing their migration and invasion potential. We propose that this may facilitate ectopic endometrial stromal invasion, explaining the development and progression of endometriosis.

**Keywords:** TGF- $\beta$ 1 EMT Peritoneum

## Poster - Pathogenesis / aetiology

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### SPARCL1, A NOVEL MOLECULE INVOLVED IN ENDOMETRIOSIS PATHOGENESIS?

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**Objectives:** To understand the mechanism involved in the onset and maintenance of endometriotic lesions regarding the expression of SPARCL1 (gene and protein) in patients with endometriosis.

**Design:** Endometrial biopsies from women without endometriosis - control group - were compared to eutopic and ectopic (peritoneal and ovarian) endometrial tissues -endometriosis group - in both proliferative and secretory phases of the menstrual cycle.

**Materials and Methods:** Samples were collected from 15 women of control group and 40 of endometriosis group (40 ectopic endometrium; 20 peritoneal and 20 ovarian endometriotic implants). Gene expression level was determined by real-time PCR, and the protein level by Western-blot. Statistical analysis was done using paired t test and Welch's ANOVA test.

**Results:** SPARCL1 gene and protein expression were shown to be more abundant in endometriotic lesions (peritoneal and ovarian) in relation to eutopic endometrium of women with and without endometriosis in both proliferative and secretory phases of menstrual cycle. SPARCL1 is also more expressed in eutopic endometrium of endometriosis patients when compared to endometrium of women without endometriosis in the secretory phase.

**Conclusion:** SPARCL1 is an extracellular matrix protein that has pro-angiogenic and anti-adhesive properties (important in proliferative and invasive tissues), which may favor endometriosis onset and development. We believe that up-regulation of SPARCL1 expression in endometriotic lesions may be responsible for the establishment and maintenance of ectopic endometrial implants.

**Keywords:** SPARCL1, deregulation, endometriosis

## Poster - Pathogenesis / aetiology

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### DIVALENT METAL TRANSPORTER-1 EXPRESSION IN THE ENDOMETRIUM OF HEALTHY WOMEN AND ENDOMETRIOSIS PATIENTS AND ITS RESPONSE TO IRON OVERLOAD AND INTERLEUKIN-1B IN ENDOMETRIAL STROMAL CELLS

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**Objectives:** To assess the iron-import protein divalent metal transporter (DMT)-1 localization and expression in the endometrium of healthy (H) women and endometriosis (E) patients throughout the menstrual cycle, and evaluating DMT-1 expression in response to iron overload and interleukin (IL)-1 $\beta$  stimuli in endometrial stromal cells (ESC).

**Design:** Endometrial biopsies were obtained from 22 H women and 22 E patients (8 proliferative, 8 secretory and 6 menstrual endometrium from each group), which were processed for immunohistochemistry and protein extraction. Isolated ESC from proliferative endometrium from 5 H women were stimulated in vitro with FeSO<sub>4</sub> and IL-1 $\beta$ .

**Materials and Methods:** DMT-1 endometrial tissue localization and expression were analyzed by immunohistochemistry and immunoblot. Proteins from cultured ESC were used to evaluate DMT-1, intercellular adhesion molecule (ICAM)-1 and light chain Ferritin (Ferr-CL) expression by immunoblot in response to iron overload (50  $\mu$ M FeSO<sub>4</sub>) and inflammatory stimuli (3 and 60 pM IL-1 $\beta$ ).

**Results:** DMT-1 localizes in glandular and stromal compartments of H and E endometrium. DMT-1 immunoblot revealed 4 variants of DMT-1: DMT80, 65, 55 and 50. DMT50 expression was lower in menstrual H and E endometrium than in proliferative ( $p < 0.01$ ) and secretory ( $p < 0.05$ ) H and E endometrium, respectively. DMT80 and DMT55 expression was increased in E versus H endometrium in most of the endometrial phases. In ESC, iron overload induced DMT80 ( $p < 0.01$ ), DMT50 ( $p < 0.001$ ) and Ferr-CL ( $p < 0.01$ ) overexpression. In response to IL-1 $\beta$  3 pM, increased protein expression of DMT80 ( $p < 0.001$ ) and DMT50 ( $p < 0.01$ ) are shown after 24 hours of stimulus. IL-1 $\beta$  induced ICAM-1 overexpression ( $p < 0.001$ ). Ferr-CL expression was reduced by IL-1 $\beta$  stimulus ( $p < 0.001$ ).

**Conclusion:** Increased DMT-1 expression in E endometrium suggests that iron incorporation could be enhanced in eutopic endometrium and in refluxed menstrual endometrium of E patients. Iron overload and IL-1 $\beta$  upregulate DMT-1 expression in ESC, possibly promoting iron influx and iron-dependent intracellular oxidative stress, inflammation and other endometriosis pathophysiologic mechanisms.

**Keywords:** DMT-1, iron, interleukin

## Poster - Pathogenesis / aetiology

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### REGULATION OF CYTOSKELETON-ASSOCIATED FACTORS BY MICRORNA MIR-142-3P IS ASSOCIATED WITH ALTERED CELL MOTILITY AND INVASIVENESS IN ENDOMETRIOSIS

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**Objectives:** microRNAs are important posttranscriptional regulators misexpressed in endometriosis. Our objective was to identify target relevant target genes and to analyze the functional impact of microRNA miR-142-3p dysregulation on endometriotic cells in vitro.

**Design:** The epithelial endometriotic cell line 12Z, the endometrial stroma cell line ST-T1b and primary eutopic and ectopic endometrial stroma cells were transfected with miR-142-3p precursors, followed by functional assays and gene expression analysis.

**Materials and Methods:** Endometriotic cells were transfected with miR-142-3p precursors. Changes in target gene expression were monitored by qPCR, 3'UTR luciferase assays and Western blotting. Cell behaviour was investigated by MTT assay, matrigel and migration assays and video microscopy. Cytoskeletal morphology was investigated by confocal immunofluorescence microscopy.

**Results:** miR-142-3p upregulation increased matrigel invasiveness and cell motility in 12Z cells, whereas motility was decreased in ST-T1b cells. Cell viability was reduced in ST-T1b cells only. miR-142-3p induced downregulation of ITGAV, Rac1, WASL and ROCK2. Cytoskeletal structure and cell size were affected by miR-142-3p, as determined by phalloidin and vinculin staining.

**Conclusion:** miR-142-3p downregulates multiple gene products involved in the cytoskeletal function and cell motility. The context-dependent impact of miR-142-3p on these processes may facilitate establishment of ectopic endometriotic lesions by promoting cellular invasiveness.

**Keywords:** microRNA, cytoskeleton, invasion

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**PHENOTYPE CHARACTERIZATION OF CONDITIONALLY REPROGRAMMED CELLS OF OVARIAN ENDOMETRIOSIS**

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**Objectives:** To develop in vitro models for functional studies of endometriosis, we established primary cultures of ovarian endometriosis obtained at the time of surgery. The use of conditionally reprogrammed cells for endometriosis has not been described before in the literature.

**Design:** Freshly isolated ovarian endometriotic tissue was co-cultured with irradiated 3T3/J2 feeder cells and the Rho kinase inhibitor Y-27632 to generate human ovarian endometriotic conditionally reprogrammed cells (CRCs).

**Materials and Methods:** We established CRCs derived from ovarian endometriomas (n=2), normal endometrium (n=5), and normal ovarian surface epithelium (n=2). Cell surface protein expression was measured by flow cytometry. Vimentin was measured by immunoblot and cytokine secretion was measured by Milliplex™ bead panel.

**Results:** In comparison to normal endometrium, the ovarian endometriomas display increased nuclear:cytoplasmic ratios and decreased growth rates. By flow cytometry, the endometriotic CRC's do not express the epithelial marker BerEP4, the ovarian markers CD105 and CD133, or the pan-leukocyte marker CD45. They are also negative for CD10 and weakly positive for CD90 (4-5%). In comparison with normal endometrial cells (n=1), we detected lower levels of IL-8 (3071pg/ml vs 0.28 pg/ml, p< 0.01) and TNF - alpha (20.31 vs 0.10, p< 0,001).

**Conclusion:** These panels of endometriotic cell lines may provide a model system for endometriosis research.

**Keywords:** Endometrioma, functional genomics

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### PEROXISOME PROLIFERATOR-ACTIVATED RECEPTOR GAMMA, COACTIVATOR 1 ALPHA (PGC-1A) STIMULATES AROMATASE IN ENDOMETRIOSIS

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**Objectives:** Estrogen is overproduced by abnormally elevated aromatase in endometriotic tissues. PGC-1 $\alpha$ , a transcriptional coactivator modulating steroid hormone, is expressed in various estrogen-dependent diseases. This study is aimed to investigate the role of PGC-1 $\alpha$  in aromatase function and its impact on local estrogen biosynthetic pathways during endometriosis.

**Design:** Experimental study in vivo and vitro

**Materials and Methods:** Primary cultured stromal cells (SCs) of ovarian endometrioma (OE), endometrium with endometriosis (EE) and normal endometrium (NE) were analyzed for PGC-1 $\alpha$ -depending changes and mechanisms in aromatase expression and function. Environmental stimulus-induced changes in PGC-1 $\alpha$  were also examined.

**Results:** PGC-1 $\alpha$  was more highly expressed in OE than in EE and NE ( $P < 0.05$ ). In OE, PGC-1 $\alpha$  coexpressed with aromatase, and mRNA expressions were correlated ( $r = 0.56$ ,  $P = 0.02$ ). ChIP-PCR revealed PGC-1 $\alpha$  recruitment to the genomic sequence containing a nuclear receptor half-site between PI.3 and PII. PGC-1 $\alpha$  overexpression enhanced aromatase promoter activity ( $P < 0.01$ ), mRNA expression ( $P < 0.05$ ), and enzymatic activity ( $P < 0.01$ ) in OESCs, but not in EESCs and NESCs. The level of PI.3, PII and exon II mRNA were increased and transcriptional enhancement was abolished by mutation of the site. PGC-1 $\alpha$  expression was enhanced in OESCs by TNF- $\alpha$  ( $P < 0.05$ ) but not by hypoxia or estradiol-17 $\beta$ .

**Conclusion:** PGC-1 $\alpha$  stimulated by TNF- $\alpha$  regulates aromatase expression and activity to promote local estrogen biosynthesis in OE, suggests that PGC-1 $\alpha$  is a promising candidate for novel targeted therapies for endometriosis.

**Keywords:** PGC-1 $\alpha$ , endometriosis, aromatase

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**IAP INHIBITOR REPRESSES CELL PROLIFERATION IN HUMAN ENDOMETRIOTIC STROMAL CELLS AND DEVELOPMENT OF ENDOMETRIOSIS IN A MURINE MODEL.**

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**Objectives:** Inhibitor of Apoptosis Protein (IAP) family: cIAP-1, cIAP-2, XIAP, and survivin, in endometriotic tissues derived from ovarian endometriomas were highly expressed compared with those in endometrial tissues. We sought to evaluate the effect of IAP inhibitor on human endometriotic stromal cells (ESCs) and on endometriosis-like lesions in a murine model.

**Design:** The effects of IAP inhibitor (BV6) on the mitogenic activity in ESCs and the efficacy on animal endometriosis model were assessed.

**Materials and Methods:** ESCs were isolated from chocolate cysts (n=20). After BV6 treatment, cell proliferation was evaluated by BrdU incorporation. E2-treated ovariectomized mice were injected intraperitoneally with endometrial fragments. After 4 weeks of BV6 injections, the endometriosis-like lesions were assessed. Proliferative and angiogenesis activities of lesions were evaluated by Ki67 and PECAM immunostaining.

**Results:** With BV6 treatment, BrdU incorporation of ESCs was significantly decreased in a dose-dependent manner. After BV6 treatment in the murine model, the total number (2.7 vs. 4.6 /mouse), the average weight (34.0 vs. 78.1 mg/mouse), and the surface area (24.6 vs. 44.5 mm<sup>2</sup>/mouse) of endometriosis-like lesions were markedly repressed compared with the control. The percentage of Ki67 positive-epithelial cells in the lesions decreased after BV6 treatment (8.8 vs. 26.8%). In addition, the intensity of PECAM positive-endothelial cells in the lesions was repressed by BV6 treatment.

**Conclusion:** IAP inhibitor could reduce cell proliferation in human ESCs and the number of lesions in the murine model. IAPs may be a potential target for the treatment of endometriosis.

**Keywords:** IAP, mouse model

## Poster - Pathogenesis / aetiology

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### STRUCTURAL MUTATION ANALYSIS OF PTEN AND ITS POSSIBLE GENOTYPE-PHENOTYPE CORRELATIONS IN ENDOMETRIOSIS AND CANCER

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**Objectives:** This proposed study explores the structural effects that the identified PTEN mutations have on the relationship between genotype and phenotype. Understanding the functional impact missense mutations have on the structure of PTEN is essential to elucidating the molecular mechanism of endometriosis and malignant transformation in the development of novel therapeutics.

**Design:** We propose that the phosphatase domain of PTEN may define a region within the active site wherein a small mutation subset possibly correlate with phenotypes. To study the influence of the mutations in greater detail, a combination of structural analysis and molecular dynamics simulations were utilized to characterize atomic interactions.

**Materials and Methods:** Utilizing structural analysis and molecular dynamics simulations, we will examine the putative effects of the clustered mutations on conformational loop distortions imposed within the active site to understand the molecular mechanism of endometriosis, endometrial and ovarian cancer. Further analysis will be conducted to investigate the possibility of correlated allosteric mutations.

**Results:** We were able to further characterize the structural effects of PTEN mutations and their role in the identified phenotypes. Each of the identified PTEN mutations were constructed and analyzed. The effects of the mutations reveal that the local structure and interactions affect polarity, conformational flexibility and electrostatic surface potential. Our data suggest that mutations within the active site disrupt the electrostatic interaction thus potentially affecting P loop conformation. One distinct residue, R130, has mutations implicated in each phenotype, a residue that potentially participates in mutation-driven allosteric regulation. In discovering the role in which PTEN contributes to the molecular mechanism of each of phenotypes, new insight into the genotypic-phenotypic correlations of endometriosis, endometrial cancer and ovarian cancer will be achieved.

**Conclusion:** The combined approaches outlined in this research have the potential of identifying the mechanistic role of PTEN associated with endometriosis, endometrial cancer and ovarian cancer. The results from our study will aid in a better clinical-molecular classification of the resulting phenotypes and allow translation into new diagnostic and therapeutic approaches.

**Keywords:** PTEN; Endometriosis; Genotype-Phenotype

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### TARGETING THE GALECTIN-1-MEDIATED ANGIOGENESIS AT PERITONEAL LEVEL CONSTRAINS THE PROGRESS OF ENDOMETRIOSIS

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**Objectives:** The endogenous lectin, Galectin-1 (Gal-1), plays a pivotal role in the vascular development and consequently growth of endometriotic lesions. A targeted blockade of Gal-1 at peritoneal level was performed with the aim to evaluate an experimental approach that could shed light on a future potential therapeutic strategy for endometriosis.

**Design:** Endometriosis was surgically induced in C57BL/6 mice by autologous transplantation of endometrial tissue to bowel mesentery. Mice were injected intraperitoneally from post-surgical day 14 and continued until day 28, 3 times a week with 15 mg/kg of the neutralizing anti-Gal-1 antibody F8.G7 (Anti-Gal-1), or with the IgG isotype antibody (Control).

**Materials and Methods:** The number and size of endometriotic lesions were evaluated in Anti-Gal-1 and Control groups at the post-surgical day 28. The relative vascularized area was assessed by immunohistochemistry in lesions and the concentrations of proangiogenic factors were measured in peritoneal fluid by ELISA, in both groups.

**Results:** Despite there was no significant difference in the number of developed endometriotic lesions between groups, notably, the peritoneal blockade of Gal-1 resulted in a significant reduction of lesions size in anti-Gal-1 treated mice compared to controls ( $P < 0.05$ ). Furthermore, the relative vascularized area immunostained for the Von Willebrand Factor, a well-known endothelial cell marker, was significantly reduced in anti-Gal-1 treated mice ( $P < 0.001$ ). However, it is important to realize that no changes were observed between groups in the relative vascularized area immunostained for the angiogenic-related Vascular Endothelial Growth Factor (VEGF) type-2 receptor. Additionally, there were no differences in the concentration of the proangiogenic factors VEGF and keratinocytes-derived CXC chemokine in peritoneal fluid between groups, suggesting that Gal-1 could be exert a direct proangiogenic effect in endometriotic lesions.

**Conclusion:** Our data highlight the potential therapeutic value of blockade Gal-1 to constrain the progression of endometriosis. These novel and promising results encourage us to emphasize efforts in order to explore the potential value of Gal-1 as an emerging therapeutic target, in order to improve the patients' clinical outcome.

**Keywords:** Galectin-1, angiogenesis, therapy.

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### SYNDECAN-4 AS A POTENTIAL PATHOGENESIS FACTOR IN ENDOMETRIOSIS

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**Objectives:** The heparan sulfate proteoglycan Syndecan-4 influences numerous cellular processes potentially relevant to the pathogenesis of endometriosis. Syndecan-4 is expressed in a menstrual-cycle specific manner. Here, the influence of Syndecan-4 on the behavior of endometriotic cells was investigated in vitro.

**Design:** In vitro experimental study in the epithelial endometriotic cell line 12Z.

**Materials and Methods:** Syndecan-4 expression was knocked down by siRNA in 12Z cells. Changes in candidate gene expression investigated by qPCR. By a matrigel invasion assay, the invasive behavior of the cells was tested. Furthermore, cell viability was assessed by MTT assay. The protein levels of target molecules were analyzed by western blotting.

**Results:** The mRNA expression of Rac1 and the transcription factor ATF2 were downregulated upon Syndecan-4 knockdown up to 50% ( $p < 0.05$ ). Syndecan-4-depleted 12Z cells were 40% less invasive compared to control cells ( $p < 0.05$ ). Syndecan-4 depletion did not alter cell viability. Focal adhesion kinase protein levels were significantly down regulated by 15% ( $p < 0.05$ ).

**Conclusion:** Syndecan-4 influences the invasive cell behavior, which may correlate to less efficient implantation of endometriotic tissue at ectopic sites in vivo. Altered function of cytoskeletal modulators contributed to the invasion phenotype of Syndecan-4 deficient cells, marking it as a potential therapeutic target.

**Keywords:** Proteoglycan, Invasiveness, cell-motility

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**17 $\beta$ -ESTRADIOL AND LIPOPOLYSACCHARIDE ADDITIVELY PROMOTE PELVIC INFLAMMATION AND GROWTH OF ENDOMETRIOSIS**

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**Objectives:** We recently demonstrated an additive effect between inflammation and stress reaction on Toll-like receptor 4 (TLR4)-mediated growth of endometriosis. Here, we investigated the combined effect between 17 $\beta$ -estradiol (E2) and lipopolysaccharide (LPS) on pelvic inflammation and growth of endometriotic cells.

**Design:** This is a case-controlled biological research with prospective collection of sera, menstrual fluid (MF), peritoneal fluid (PF) from 46 women with endometriosis and 30 control women and their retrospective evaluation. Peritoneal macrophages (M $\phi$ ) and eutopic/ectopic endometrial stromal cells (ESCs) were isolated in primary culture.

**Materials and Methods:** Concentrations of E2 and progesterone (P) were measured in body fluids. Cytokine secretion by M $\phi$  and proliferation of ESCs in response to E2 and LPS were measured by ELISA and by bromodeoxyuridine incorporation assay, respectively. A blocking experiment was performed using respective antibodies against estrogen receptor (ER) and TLR4.

**Results:** No significant difference in E2 and P concentrations was observed in different body fluids between women with and without endometriosis. A significantly increased secretion of interleukin (IL)-6 and tumor necrosis factor alpha (TNF $\alpha$ ) in M $\phi$  culture media was found in response to E2 (10<sup>-8</sup>M) comparing to non-treated M $\phi$ . This effect of E2 was abrogated after pre-treatment of cells with ICI (10<sup>-6</sup>M), an estrogen receptor (ER) antagonist. An additive effect of E2 on the LPS (10ng/mL)-activated secretion of IL-6 and TNF $\alpha$  by M $\phi$  was observed. Combined treatment with E2 and LPS further promoted cytokine secretion in culture media and growth of eutopic/ectopic ESCs. The additive effect of E2+LPS was effectively suppressed after combined blocking of ER and TLR4.

**Conclusion:** An immuno-endocrine crosstalk was observed between E2 and LPS in promoting pro-inflammatory response in pelvic environment and growth of endometriotic cells. Our findings may provide some new evidence to understand the role of more than a single factor in pelvis in inducing inflammation and promoting growth of endometriosis.

**Keywords:** Endometriosis, estrogen, lipopolysaccharide

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**OVARIAN SUPERFICIAL ENDOMETRIOSIS MAY FACILITATE FORMATION OF OVARIAN ENDOMETRIOMA: A HISTOLOGICAL ANALYSIS.**

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**Objectives:** The pathogenesis of ovarian endometrioma is still controversial. Formation of endometrioma may affect the function of surrounding ovarian cortex, and may be related to loss of ovarian reserve. In this study, we performed histological analysis of superficial ovarian endometriotic lesion in relation to formation of endometrioma and homeostasis of follicles.

**Design:** Histological analysis of biopsied samples of ovarian cortex derived from women with endometriomas.

**Materials and Methods:** Forty women with ovarian endometriosis had biopsy of ovarian cortex at laparoscopy. Tissue was fixed in Bouin's solutions and serial sections were made perpendicular to ovarian axis. Thirteen cortical samples with superficial endometriosis with glandular epithelium and stromal component were selected. Hematoxylin and eosin, Masson trichrome, and immunohistochemistry were performed.

**Results:** Superficial endometriotic lesion showed positive staining for cytokeratin cocktails and CD10. Cytokeratin positive epithelia were negative for calretinin stain that was immunoreactive to normal ovarian surface epithelium (OSE). Ovarian cortical tissue surrounding endometriotic lesion showed marked fibrosis and infiltration of CD68-positive macrophages. Invagination and aberration of calretinin-positive surface epithelia were evident under fibrosis. Inclusion cyst with cytokeratin positive cell lining was detected. Primordial follicles in surrounding cortex frequently showed morphologically atretic features.

**Conclusion:** Origin of superficial ovarian endometriotic lesion may be similar to peritoneal endometriosis. Progression of these lesions along with reactive inflammation in surrounding ovarian cortex may induce fibrosis with concurrent inclusion of OSE and metaplasia resulting in cyst formation. The inflammation in ovarian cortex may adversely affect homeostasis of dormant follicles.

**Keywords:** Endometrioma inflammation atresia

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**EXPRESSION OF ENZYMES INVOLVED IN LOCAL REGULATION OF SULFONATED ESTROGENS IS DYSREGULATED IN ENDOMETRIUM OF WOMEN WITH ENDOMETRIOSIS**

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**Objectives:** Steroid sulfatase (STS) and estrogen sulfotransferase (EST) are enzymes that promote continuous renewal of circulating sulfonated estrogens in target tissues. Since endometriosis can be influenced by the enzymes that regulate the availability of estrogens, we investigate the expression and regulation of STS and EST in the endometriosis context.

**Design:** This cross-sectional study used endometria and endometriotic lesions from women (n=78) with endometriosis and healthy endometrium collected from women that underwent tubal ligation (controls, n=15). Menstrual phase was determined by the reported cycle day and the circulating concentrations of progesterone (luteal phase: >1ng/ml and follicular phase: <1ng/ml).

**Materials and Methods:** In situ and in vitro expression of STS and EST were evaluated by real time PCR using Genorm for normalization. Data was log transformed and an ANOVA with Tukey post-test was used to test for differences between expressions in eutopic, ectopic (superficial and deep lesions), and healthy endometria.

**Results:** Results indicated that EST and STS did not change in the endometrium of women with endometriosis when compared to controls, neither in the secretory (P=0.71) or follicular phases (P=0.92). However, there was a consistent increase in STS expression in superficial and deep-infiltrating endometriotic lesions as compared to endometrial samples. Estrogen sulfotransferase expression was likewise higher in endometriotic lesions, but with a distinct increment in deep-infiltrating endometriosis. Interestingly, for the first time the actions of female steroid hormones on EST and STS expression were evidenced in endometriosis, as revealed by increased expression levels in lesions collected in the secretory phase of the cycle. This finding agreed with Western Blot analysis, especially for STS expression.

**Conclusion:** This suggests that a constant sulfonation coupled with desulfonation might occur in lesions of endometriosis patients, especially deep-infiltrating lesions in the secretory phase. The observed differential regulation of STS and EST may support studies on the therapeutic potential of the use of STS inhibitors in endometriosis. Thanks to FAPESP (2010/02412-6).

**Keywords:** Sts, est, sult1e1

## Poster - Pathogenesis / aetiology

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### HYPOCORTISOLISM IN ENDOMETRIOSIS PATIENTS

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**Objectives:** Assess the relationships between cortisol levels and perceived stress, coping styles and years with symptoms in endometriosis patients compared to healthy women. We hypothesized that patients would report higher stress and show lower cortisol levels than controls, and that cortisol would correlate with coping styles and years with symptoms.

**Design:** The experiment was a case control study.

**Materials and Methods:** Cortisol was measured in saliva samples collected from 31 endometriosis patients and 36 controls using an immunoassay kit. Subjects completed a stress checklist, the State/Trait anxiety inventory, and a coping skills survey. Patients also completed a pain scale and quality of life survey. Statistical analyses were performed using SPSSv17.

**Results:** Patients with endometriosis had an average salivary cortisol concentration of 508.6 pg/ml, while controls had an average of 1056 pg/ml ( $p < 0.0057$ ). A negative correlation was found between cortisol level and infertility ( $p < 0.0195$ ) and dyspareunia ( $p < 0.0254$ ). Correlational analyses were performed between cortisol and dysmenorrhea, perceived stress, coping skills, and years with symptoms, but none were significant. There was a significant difference in Trait Anxiety scores between patients and controls, however this was not correlated to cortisol concentration.

**Conclusion:** This study supports the notion of hypocortisolism in endometriosis. However, there was no correlation with years experiencing symptoms, which suggests that 1) hypocortisolism is due to underlying genetic factors predisposing to impaired HPA responses, or 2) in endometriosis patients even short exposures to pain can negatively affect HPA axis functioning.

**Keywords:** Endometriosis, Cortisol, HPA-axis

## Poster - Pathogenesis / aetiology

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### BONE-ASSOCIATED MOLECULAR PATHWAYS IN ENDOMETRIOSIS

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**Objectives:** Microarrays reveal several factors usually seen in bone over-represented in endometriosis. Cytokines that regulate these pathways such as TGFβ1 and BMP are also increased in lesions. Because TGFβ1 and BMP-2 are key regulators of osteogenesis, we hypothesised that these cytokines may stimulate bone-associated molecular pathways in eutopic and ectopic endometrium.

**Design:** Primary human endometrial fibroblasts (HEF) were isolated from endometrial tissue of women undergoing laparoscopy for endometriosis symptoms (n=10). Paired eutopic and ectopic tissues were fixed, embedded in paraffin wax and cut in 5µm sections.

**Materials and Methods:** HEF were treated with 0.05-50ng/mL TGFβ1, BMP-2 or vehicle, and total RNA extracted or media collected 24hr later. Bone-associated factors were assessed by qRT-PCR, ELISA or Luminex assay. Eutopic and ectopic sections were stained with Alizarin Red to detect dystrophic calcification.

**Results:** At the mRNA level, TGFβ1 decreased osteoprotegerin, dermatopontin and IGFBP5, and increased Dlx5, TGFβ1 and Runx2 in primary HEF (P<0.05, t-test), whereas periostin, osteopontin, osteonectin, matrix Gla protein, versican, Msx1, and fibromodulin were not affected. TGFβ1 dramatically decreased periostin concentration in conditioned media and modestly decreased osteopontin in time and/or dose dependent fashion (P<0.05, 2-way ANOVA). Osteoprotegerin protein production was also decreased by TGFβ1 (P<0.001, t-test). BMP-2 decreased osteopontin and increased periostin protein concentration (P<0.05, 2-way ANOVA), but only at the highest dose tested. Dystrophic calcification including psammoma bodies was detected in several ectopic tissues examined, but not in eutopic endometrium.

**Conclusion:** These data suggest that bone-associated factors can be regulated TGFβ1 and BMP-2 in endometrial tissues. Abnormal activation of these pathways may influence the formation of psammoma bodies. We speculate that these structures inhibit normal immune clearance of refluxed tissue from the peritoneal cavity, contributing in some women to disease persistence.

**Keywords:** TGFbeta1, cytokines, calcification

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**EXPRESSION OF SMAD 3, PHOSPHORYLATED SMAD 3 AND SMAD 4 IN THE ENDOMETRIUM OF WOMEN WITH AND WITHOUT ENDOMETRIOSIS**

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**Objectives:** Smads are proteins which mediate the signaling of members of the TGF-beta superfamily. The aim of the present study was to evaluate the endometrial gene expression of Smad 3 and Smad 4 and the immunostaining of Smad 3, phosphorylated Smad 3 and Smad 4 in women with endometriosis.

**Design:** This was a case control study.

**Materials and Methods:** Using real-time PCR and immunohistochemistry, the endometrial expression of Smads 3 and 4 and the localization of Smad 3, phosphorylated-Smad 3 and Smad 4 were investigated in women with (n=9) and without (n=6) endometriosis. The immunostaining was scored using an automated software and the results were analyzed using Mann-Whitney test.

**Results:** The gene expression of Smad 3 and Smad 4 was similar in cases and controls. Smad 3, phosphorylated-Smad 3 and Smad 4 immunostaining were both cytoplasmic and nuclear and were present in the glandular epithelium and stroma. We found a median decrease of 2/3 in the intensity of Smad 3 immunostaining in the endometriosis group compared to controls (4 vs 12 arbitrary units, p=0.017), whereas no significant changes were found in the cytoplasmic staining of phosphorylated-Smad 3 or in the nuclear staining of Smad 4.

**Conclusion:** Smad proteins might be altered in the endometrium of women with endometriosis, although this imbalance spared the end point represented by nuclear Smad 4. Due to the critical role of TGF-beta superfamily growth factors in endometrial growth and differentiation, this signaling system might provide candidate molecular targets to treat endometriosis.

**Keywords:** Endometrium; Endometriosis; Smads

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### EVALUATION OF CELL DIFFERENTIATION AND TISSUE INVASION MARKERS IN TOPIC AND ECTOPIC ENDOMETRIUM IN A RABBIT EXPERIMENTAL MODEL OF ENDOMETRIOSIS.

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**Objectives:** To characterize the pattern of differentiation and tissue invasion on topic and ectopic endometrium of rabbits with induced endometriosis, four and eight weeks after the endometrial implantation procedure in order to characterize the histological evolution of the lesions.

**Design:** Prospective experimental model using a rabbit experimental model.

**Materials and Methods:** 29 rabbits were submitted to laparotomy for induction of endometriosis. They were divided into two groups: group 1 was sacrificed after 4 weeks of induction and, group 2 with 8 weeks. The lesion was excised for histological analysis along with the contralateral uterine horn. Immunohistochemical reactions were performed.

**Results:** There was a higher immunostaining for MMP 9, TIMP 2, Metallothionein and p63 in ectopic tissue compared with eutopic endometrium. However, when the ectopic lesions of 4 and 8 weeks were compared no significant difference was observed, with the exception of the marker p63, which was more evident after 8 weeks of evolution of the ectopic endometrial tissue.

**Conclusion:** The ectopic lesions seem to express increased cell differentiation and tissue invasion when compared to eutopic endometrium, featuring endometriosis as a disease potentially invasive, progressive and heterogeneous in its presentation.

**Keywords:** Endometriosis, MMP9, p63

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**HMGB-1 INDUCED TOLL-LIKE RECEPTOR 4 SIGNALING PROMOTES CELL PROLIFERATION IN ENDOMETRIAL STROMAL CELLS.**

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**Objectives:** Toll-like receptors (TLRs) are innate immune receptors that mediate the pattern recognition of, and response toward, pathogens and host-derived danger signals. We examined whether endogenous ligands released by damaged cells such as high-mobility group box-1 (HMGB-1) signaling through TLR4 may play a pathogenic role in endometriosis.

**Design:** The effects of HMGB-1-TLR4 signaling on endometrial stromal cell proliferation was examined. Specific inhibitor of NF- $\kappa$ B signaling pathway was used to explore the role of NF- $\kappa$ B signaling pathway in HMGB-1-TLR4 pathway

**Materials and Methods:** HMGB-1 and TLR4 expression in endometrium were analyzed using immunohistochemistry. Real-time PCR was used to quantify TLR4 mRNA levels and western blotting was used to verify TLR4 protein.

**Results:** During the menstrual cycle, TLR4 protein was highly expressed. HMGB-1 significantly enhanced cell proliferation in human endometrial stromal cells (HESCs) with TLR4 dependent. Small interfering RNA experiments confirmed the association between TLR4 and proliferation induced by HMGB-1 in HESCs. HMGB-1-TLR4 signaling was associated with regulation on the activation of NF- $\kappa$ B signaling pathway.

**Conclusion:** Our results suggest that HMGB-1-TLR4 signaling may play an important role in establishment of endometriosis through NF- $\kappa$ B signaling pathway.

**Keywords:** HMGB-1, Endometriosis, TLR4

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### BIOINFORMATIC ANALYSIS OF SIGNALING PATHWAYS INVOLVED IN DEVELOPMENT OF ENDOMETRIOSIS.

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**Objectives:** To identify intracellular factors responding to extracellular stimuli involved in endometriosis and to find the perspective targets for therapy based on networks of signaling pathways.

**Design:** Complex review of intra- and extracellular factors that have been reported to be aberrantly expressed in endometriosis, bioinformatic analysis by MetaCore software and a network of signaling pathways underlying elevated capacity of ESCs to proliferation, migration, and surviving of endometrial lesions.

**Materials and Methods:** Review of pubmed- and clinicalkey-listed articles about endometriosis, bioinformatic analysis of signaling pathways by MetaCore software.

**Results:** According to the analysis of intracellular signalling pathways, endometriosis is a complex disease including abnormal activation of several intracellular pathways, such as Jak/STAT, TGF-beta/SMADs, SAPK/JNK, MAPK, WNT/Beta-catenin, NF-kB, PI3K/AKT which determine aberrant cellular processes responsible for the development and progression of endometriosis. and interact at key transcription factors, that need to be investigated in further studies and could be used for targeted therapy.

**Conclusion:** Endometriosis is an enigmatic disease with complex aetiology and pathogenesis. Despite a huge amount of development factors leading to endometriosis, there is a common pattern of intracellular aberrants, which cause an increased cell migration, adhesion, proliferation, angiogenesis, survival of ESCs and their capacity.

**Keywords:** Endometriosis, signaling pathways

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### DEEP OVARIAN ENDOMETRIOSIS - A DISTINCT HISTOLOGICAL PATTERN

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**Objectives:** Some authors consider ovarian endometriosis a marker of extensive disease. Ovarian endometriosis divides in two histological types: cystic and intraparenchymatous, also described as deep invasive ovarian endometriosis. We aim to investigate the association of each type with clinical features and location of disease.

**Design:** Cross-sectional study of patients submitted to laparoscopy to treat ovarian endometriosis.

**Materials and Methods:** Between January 2008 and June 2012, 250 women have undergone laparoscopic treatment to ovarian endometriosis. We compared pre-operative clinical symptoms and the presence of other locations of disease between cystic and intraparenchymatous groups.

**Results:** We identified cystic endometriosis in 196/250 (78.4%) women, while intraparenchymatous in 54/250 (21.6%). Although, 70.6% (36/51) patients with intraparenchymatous type had deep dyspareunia, it was similar to the cystic pattern (57.3%;  $p=0.0848$ ). Dysmenorrhea, acyclic pelvic pain, infertility, cyclic intestinal and urinary symptoms were similar in the cystic and intraparenchymatous groups (59.7% x 49%,  $p=0.1647$ ; 17.3% x 25.9%,  $p=0.1564$ ; 57.1% x 70.6%,  $p=0.1556$ ; 29.6% x 40.7%,  $p=0.1199$ ; 10.7% x 16.7%,  $p=0.2333$ , respectively). We found a similar involvement of peritoneum, retrocervix, rectum-sigmoid, appendix, ileum, vagina, bladder and ureter in cystic and intraparenchymatous endometriosis (44.4% x 55.5%,  $p=0.1453$ ; 44.9% x 38.9%,  $p=0.4304$ ; 36.2% x 46.3%,  $p=0.1778$ ; 8.7% x 3.7%,  $p=0.2224$ ; 3% x 3.7%,  $p=0.8123$ ; 6.1% x 11.1%,  $p=0.2092$ ; 7.6% x 5.5%,  $p=0.5975$ ; 5.1% x 9.3%,  $p=0.2547$ , respectively).

**Conclusion:** Intraparenchymatous endometriosis is less frequent than the cystic form. Intraparenchymatous type is histologically distinct from the cystic pattern, although, does not seem to correlate with clinical symptoms and extent of disease. Further studies with markers of cell proliferation and apoptotic regulation could provide insights on its differences and repercussions.

**Keywords:** Intraparenchymatous, cystic, endometriosis

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### ALTERATIONS OF LDL-C LEVELS IN PATIENTES WITH DEEP INFILTRATIVE ENDOMETRIOSIS.CAN THE DISEASE ENHANCE CHOLESTEROL CONSUMPTION ?

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**Objectives:** Analyze the lipid profile and concentration of apolipoproteins A1 and B100 in patients with deep infiltrative endometriosis affecting the bowel.

**Design:** Case-control prospective study in 2 groups of patients, with and without endometriosis. Blood was collected before the surgical procedure in 20 patients diagnosed with deep infiltrative endometriosis affecting the bowel, after a hormonal wash-out of 3 months and in 20 patients assigned to tubal ligation.

**Materials and Methods:** Total cholesterol, HDL-c and triglycerides concentrations were determined by enzymatic-colorimetric assay kits. LDL-c concentration was calculated by Friedewald formula. Serum concentrations of apolipoprotein A1 and apolipoprotein B100 were determined by the immunoturbidimetric method. Statistical analysis was performed by Student t-test. Difference of  $p < 0.05$  was considered statistically significant.

**Results:** LDL-c concentration was lower in endometriosis group when compared to control group ( $122 \pm 24$  vs  $151 \pm 40$  mg/dL) ( $p = 0.0073$ ). Both endometriosis group and control group showed no difference in concentrations of total cholesterol ( $191 \pm 28$  vs  $189 \pm 39$  mg/dL), HDL-c ( $43 \pm 9$  vs  $43 \pm 13$  mg/dL), triglycerides ( $133 \pm 41$  vs  $117 \pm 52$  mg/dL), apoA1 ( $129.5 \pm 31.7$  vs  $136.1 \pm 17.7$  mg/dL) and apoB100 ( $77.6 \pm 20.7$  vs  $89.3 \pm 30.1$  mg/dL).

**Conclusion:** Patients with endometriosis showed lower LDL-c concentration compared to control group, suggesting a higher uptake of LDL by the endometriotic tissue. The increased LDL uptake may be ascribed to accelerated cell proliferation.

**Keywords:** deep endometriosis; LDL-c

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### ASSOCIATION OF SUB-CLINICAL VAGINAL INFECTION IN WOMEN WITH ENDOMETRIOSIS

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**Objectives:** We previously reported higher bacterial contamination of menstrual blood and effect of bacterial endotoxin (lipopolysaccharide, LPS) on pelvic inflammation and growth of endometriotic cells. However, a possible involvement of sub-clinical vaginal infection in women with endometriosis is still unknown. Here we investigated this unclear clinical issue in women with endometriosis.

**Design:** This is a case-controlled clinico-biological research with prospective collection of vaginal/cervical/endometrial smears and eutopic endometria during laparoscopy from 73 women with endometriosis and 65 women without endometriosis and their retrospective evaluation.

**Materials and Methods:** Intra-vaginal pH was measured using pH paper strip. A Gram-staining was performed in all vaginal smears for the analysis of bacterial vaginosis (BV) according to Nugent score. By immunohistochemistry, CD138-stained plasma cells and myeloperoxidase-stained neutrophils were analyzed in endometrial samples for the identification of chronic or acute endometritis.

**Results:** Although no significant difference was observed in vaginal pH (<4.5 vs. >4.5) and BV score (7-10) between control and women with endometriosis, a significant shifting of vaginal pH to >4.5 ( $p=0.03$ , X2 test) and increased harboring of intermediate flora (Nugent score, 4-6) ( $p=0.05$ , X2 test) were found in women with endometriosis after GnRHa treatment. Concurrently, normal vaginal flora (Nugent score, 0-3) was remarkably altered in women with and without endometriosis after GnRHa treatment. This adverse effect of GnRHa on microbial colony corresponded with higher occurrence of acute endometritis in women with endometriosis. Phases of menstrual cycle and revised-ASRM staging of endometriosis did not influence this effect in GnRHa-non-treated women. A relationship between intra-vaginal microbial environment and endometrial microbial colonization will be discussed.

**Conclusion:** Our findings suggest that women with endometriosis may be associated with sub-clinical vaginal infection. Estrogen suppressing agents traditionally used for the treatment of endometriosis may worsen microbial colonization in vaginal /endometrial environment resulting in the occurrence of endometritis. Our findings may hint future therapeutic prospect in women with endometriosis.

**Keywords:** endometriosis, BV, endometritis

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### CCN FAMILY IN ENDOMETRIOTIC TISSUES: A DEREGULATED NETWORK TOWARDS FIBROTIC PHENOTYPE

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**Objectives:** The CCN family (CCN1-6: CYR61, CTGF, NOV, WISP1-3) is composed of six matricellular proteins that have important roles in cellular processes. The aim of the study was to examine the mRNA and protein expression of the CCN family members in endometriotic tissues from endometriosis-affected woman as compared to controls.

**Design:** A case-control laboratory study in a tertiary-care university hospital. Quantitative RT-PCR and immunohistochemistry were performed to investigate the differential mRNA and protein expression in 51 women, with (n=26) and without (n=25) endometriosis.

**Materials and Methods:** CCN family members mRNA expression was investigated by quantitative RT-PCR in 15 endometrium of disease-free women, 16 eutopic and 16 ectopic endometrium of endometriosis-affected women. CCN1, CCN3, CCN4 and CCN6 expression was explored by immunohistochemistry in 10 endometrium of disease-free women and 10 eutopic and ectopic endometrium of endometriosis-affected women.

**Results:** In ectopic endometrium of endometriotic women, expression of CCN1, CCN2, CCN4 and CCN5 was significantly increased as compared to endometrium from disease-free women (3.8-fold, 2.4-fold, 5.2-fold, and 91.4-fold respectively; p<0.05). Conversely, CCN3 was significantly decreased in ectopic endometrium as compared to endometrium from disease-free women (4.2-fold, p<0.05). CCN6 expression was only slightly increased in ectopic endometrium without reaching statistical significance. On immunolabelling, CCN1, CCN3, CCN4 and CCN6 display a strong epithelial and stromal staining in ectopic endometriosis tissues.

**Conclusion:** This study, for the first, time reveals a significant deregulation of the CCN protein network in the ectopic endometrium of women with endometriosis. Interestingly, our results support a model in which the CCN action in ectopic endometriotic lesions is tuned towards a fibrotic phenotype.

**Keywords:** Endometriosis CCN\_family fibrosis

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**HISTOLOGIC CLASSIFICATION OF ENDOMETRIOSIS: INCREASED EXPRESSION OF BCL-2 IN WELL-DIFFERENTIATED GLANDULAR ENDOMETRIOSIS IN BOWEL LESIONS**

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**Objectives:** Investigate cellular apoptosis of deep bowel lesions and correlate findings with the four histological types identified in endometriotic implants, to that's why the antiapoptotic factor Bcl-2 and the pro-apoptotic Bax factor were used as markers of apoptosis.

**Design:** Observational cross-sectional study with pathological analysis

**Materials and Methods:** Thirty-three women with bowel endometriosis was treated with laparoscopic colorectal resection in tertiary referral university hospital. After confirming the diagnosis of endometriosis, the morphological classification of the lesion was performed, considering the four types. For immunohistochemical analysis, the sections were incubated with Bcl-2 and the Bax antibodies

**Results:** It was found a predominance of mixed glandular endometriosis, present in 15 specimens (45.4%), followed by the undifferentiated glandular endometriosis with nine (27.2%) and the well-differentiated glandular endometriosis identified in eight (24.2%) out of the 33 specimens of the bowel lesions. Well-differentiated glandular endometriosis had significantly higher immunoexpression of Bcl-2 compared to undifferentiated glandular endometriosis ( $p=0.01$ ). Bax expression was null in all histological endometriosis types in qualitative terms.

**Conclusion:** These findings suggest that well-differentiated glandular endometriosis is the histological type with the biggest activity since it has the greatest impact on cellular apoptosis.

**Keywords:** Apoptosis; Endometriosis, Classification.

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### EXPERIMENTAL MODEL OF INTESTINAL ENDOMETRIOSIS IN PIGS

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**Objectives:** Experimental models of endometriosis use autologous tissue transplantation, with topic endometrium resected and usually implanted in the peritoneum. Our objective is to create an experimental model of intestinal endometriosis in pigs

**Design:** Experimental study using two sexually mature female minipigBR pigs

**Materials and Methods:** We performed two laparotomies in each animal. The first one to create the intestinal endometriosis implants. The second one was performed thirty days latter to visualize, measure the implants and obtain tissue for histopathology study

**Results:** In the first laparotomy a 5-cm segment of right uterine horn was resected. The endometrium was separated from the myometrium through subendometrial saline injection. Fragments (1.0 x 2.0 cm) were sutured in rectum of the animals. The remaining of the endometrium was sent to histopathology analysis. The histopathology analysis demonstrated proliferative endometrium in all animals. “En-bloc” resection of the intestinal segment and the endometriosis implants was performed in the second surgery. The histopathology analysis of the specimen resected in the second surgery showed invasion of the muscularis propria layer of the rectal wall in 1 of 2 animals

**Conclusion:** The creation of an animal model of deep infiltrating endometriosis with intestinal involvement is feasible through a simple surgical technique

**Keywords:** Intestinal, endometriosis, experimental

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### DO CHOCOLATE FLUIDS TELL US ANYTHING ABOUT THE HISTORY OF OVARIAN ENDOMETRIOMAS

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**Objectives:** To test the hypotheses that 1) older endometriomas contain fluid with higher ferritin or free iron content than younger ones due to gradual accumulation of red blood cells; 2) since repeated injury leads to tissue fibrosis, older cysts have higher collagen content and more adhesions than younger ones.

**Design:** Cross-sectional studies of endometriotic lesion histology, coloration, and of chocolate fluid harvested from 34 pre-menopausal women (mean age=32 (SD=7.1) years) with histologically confirmed ovarian endometriomas. Among the 34 endometrioma cysts, 15 (44.1%) were black or brown colored, and the remaining 19 (55.9%) were white---considered to be older endometriotic lesions.

**Materials and Methods:** The viscosity, density, and the concentration of total bilirubin, ferritin, and free iron of the chocolate fluid were measured. The lesion color and adhesion score were also recorded. In addition, we performed Masson trichrome staining on the endometriotic cysts.

**Results:** Fluids taken from white-colored endometriomas had significantly higher concentration of total bilirubin ( $p=0.016$ ), ferritin ( $p=0.0035$ ), and free iron ( $p=0.0045$ ), respectively, than black/brown-colored ones. In addition, older cysts had fluids that had significantly higher density ( $p=1.3 \times 10^{-5}$ ) and viscosity ( $p=0.0002$ ). The cyst size was not correlated with the cyst coloration, bilirubin, ferritin or iron content, or with density or viscosity. We also found that the density of the chocolate fluid correlated positively with the concentrations of total bilirubin, ferritin, and free iron (all  $p$ -values  $< 0.05$ ). White-colored endometriomas had significantly higher Masson staining scores and adhesion scores ( $p=0.011$  and  $p=0.005$ , respectively), suggesting that indeed these lesions did have higher fibrotic content, a result of cyclic and repeated injury and healing.

**Conclusion:** Older cysts have more bleeding episodes and higher fibrotic content resulting from repeated injury and healing. This study provides another piece of evidence that endometriotic foci are wounds that undergo repeated injury and healing, resulting ultimately in fibrotic lesions with extensive adhesions, explaining as why endometriosis is tough to treat.

**Keywords:** Endometrioma; fibrosis; history

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### GALECTIN-3 CONTRIBUTES TO THE DEVELOPMENT OF ENDOMETRIOSIS

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**Objectives:** To evaluate the differences between the endometric lesions developed in wild type mice (WT) and mice deficient in galectin-3 (Gal-3 <sup>-/-</sup>), a member of the  $\beta$ -galactoside-binding soluble lectin family that regulates cell proliferation, differentiation, apoptosis and angiogenesis in both normal and tumor tissues.

**Design:** The study was developed using an animal model of endometriosis.

**Materials and Methods:** Endometriosis experimental model was developed in wild type mice and mice deficient in galectin-3. The development of lesions was examined as well as the morphology of these lesions. Furthermore, angiogenesis and inflammation processes were investigated by western blot, flow cytometry analysis and differential leucocytes count.

**Results:** The morphological analyzes showed growth of endometrial implants, presence of glandular structures and regular endometrial stroma in both animal models, nonetheless the endometriotic lesions were bigger in WT when compared with Gal-3 <sup>-/-</sup> animals. Analysis of protein expression showed a higher expression of vascular endothelial growth factor (VEGF) and its receptor Flk-1 and a reduced expression of cyclooxygenase-2 in WT endometriotic lesions when compared with Gal-3 <sup>-/-</sup> endometriotic lesions. The analysis of peritoneal macrophages revealed a greater presence of these cells in the peritoneal fluid of WT mices, corroborating with the literature data that indicate an important role of macrophages in the development of endometriosis. However, no differences were observed in total leukocyte count.

**Conclusion:** This data indicate an important role of galectin-3 in endometriosis development, since the lack of this molecule led to less development of this pathology.

**Keywords:** Endometriosis, galectin-3, macrophages

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### INHIBITION OF TUMOUR NECROSIS FACTOR A INDUCED IKK $\beta$ ACTIVITY IN EPITHELIAL ENDOMETRIOTIC CELLS ATTENUATES CYTOKINE PRODUCTION, BUT STIMULATES CELL PROLIFERATION

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**Objectives:** Endometriosis is an inflammatory condition accompanied by increased peritoneal fluid (PF) cytokine concentrations that stimulate lesion progression. IKK $\beta$  is a key molecule that links inflammation to tumour progression through multiple signalling pathways. We wish therefore to understand the role of IKK $\beta$  in endometriotic lesion progression.

**Design:** Endometriotic tumour tissue and peritoneal fluid was collected during laparoscopic surgery and analysed for IKK $\beta$  expression and cytokine concentrations respectively. The effect of IKK $\beta$  inhibition in vitro was determined with primary endometrial stromal cells (ESC) and endometriotic epithelial cells (12Z).

**Materials and Methods:** Cellular expression of total IKK $\beta$  and pIKK $\alpha/\beta$ (Ser176/180) in endometriotic tumour tissue was determined via immunohistochemistry and concentrations by semi-quantitative Western blotting. In vitro IKK $\beta$  inhibition was achieved with PS-1145 and TPCA and the resulting cytokine concentrations measured by ELISA and cellular proliferation by an MTS assay.

**Results:** IKK $\beta$  was present in both stromal and epithelial cells, however pIKK $\alpha/\beta$ (Ser176/180) was predominantly epithelial. A significant, positive correlation between peritoneal fluid TNF $\alpha$  and pIKK $\alpha/\beta$ (Ser176/180) ( $r = 0.5901$ ,  $p = 0.0161$ ,  $n = 16$ ) and a relationship approaching significance with IKK $\beta$  ( $r = 0.4987$ ,  $p = 0.0585$ ,  $n = 15$ ) in endometriotic lesions was observed. In vitro experiments indicated strong pIKK $\alpha/\beta$ (Ser176/180) expression in 12Z cells, but only weak expression in ESC. Inhibition of IKK $\beta$  activity significantly decreased IL-8 ( $p < 0.0001$ ) and MCP-1 ( $p < 0.0001$ ) production in the epithelial 12Z cell line, but not the ESC. Conversely, IKK $\beta$  inhibition also resulted in a concentration dependent increase in cellular proliferation of the 12Z cells and to a lesser extent in the ESC cells.

**Conclusion:** IKK $\beta$ , an important regulator of inflammation-stimulated growth, is activated in epithelial endometriotic cells by TNF $\alpha$ . Inhibition of IKK $\beta$  can attenuate the inflammatory reaction of epithelial cells, but conversely leads to an increase in cell proliferation. Aberrant activity of IKK $\beta$  in endometriotic epithelial cells may contribute to endometriosis pathogenesis.

**Keywords:** IKK $\beta$ , inflammation, proliferation

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### **SURGICALLY INDUCED ENDOMETRIOSIS IN A CYNOMOLGUS MONKEYS(MACACA FASCICULARIS)**

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**Objectives:** To establish an experimental model in cynomolgus monkeys for the study of endometriosis.

**Design:** The experimental study was approved by the animal experiment committee at Tsukuba Primate Research Center, Japan. Nodular and superficial endometriosis was induced in cynomolgus by grafting autologous uterine endometrium onto the peritoneum and by scattering minced endometrium in the peritoneal cavity.

**Materials and Methods:** 16 female cynomolgus monkeys with a mean age of 11.0 years (range 6–18) were inoculated to establish lesion induction. After surgery, the lesions were evaluated by laparoscope and were measured by MRI. Induced lesions were identified by histological evaluation with immunohistochemical analysis.

**Results:** The general condition of the monkeys did not change after surgery. After 1 month, the incidence of induced nodular endometriosis was 100%, and of superficial endometriosis was 69%. Nodular lesions included chocolate cystic components. Microscopic lesions induced after grafting endometrium showed endometriosis, characterized by scattered glands with CD10-positive stroma. Lesions also revealed angiogenesis and thickened interstitium by fibrosis.

**Conclusion:** We have developed an experimental model in cynomolgus monkeys. Endometriosis in the experimental model mimics the disease progression in spontaneous endometriosis. This experimental model is a versatile model that can be used to study the immune system, hormones, and environmental factors of endometriosis.

**Keywords:** Cynomolgus monkeys, endometriosis

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### ANALYSIS OF WNT4 MRNA EXPRESSION IN WOMEN WITH ENDOMETRIOSIS

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**Objectives:** WNT4 is a protein concerned with multiple processes in organ development including reproductive tissues, and involved in proliferation, differentiation and maintenance of endometrium. Endometriosis is a disease characterized by the presence of endometrial cells in the extra-uterine environment. This study was designed to assess how Wnt4 is involved in endometriosis.

**Design:** We analyzed expression of Wnt4 mRNA of eutopic endometrium, endometrial cyst and peritoneal endometriosis of women with endometriosis grouped by r-ASRM classification. eutopic endometrium of women with uterine myoma were analysed as non-endometriosis control. All experimental procedures were reviewed and approved by the Ethics Committee of Nippon Medical School.

**Materials and Methods:** Total mRNA of eutopic endometrium of women with non-endometriosis or with endometriosis, endometrial cyst and peritoneal endometriosis was extracted, cDNA was synthesized and qPCR was performed. Wnt4 mRNA expression of endometrial glandular or stromal cells assayed using laser assisted microdissection. Women with endometriosis were grouped using r-ASRM classification of endometriosis.

**Results:** The expression levels of Wnt4 mRNA in eutopic endometrium of women with endometriosis classified into stage III were no significant difference compared to those of controls, while those of women grouped into stage IV were significantly higher than those of controls. However, the expression levels of Wnt4 mRNA in endometrial cyst were significantly higher than those in eutopic endometrium of women grouped into stage III. There were no significant differences between endometrial cyst and eutopic endometrium in women grouped into stage IV. The expression levels of Wnt4 mRNA in peritoneal endometriosis were significantly higher than those in endometrium of controls. The expression of Wnt4 mRNA was mainly localized in endometrial stromal cells, had a tendency toward increase in endometrial cyst than in eutopic endometrium.

**Conclusion:** Taken together the expression levels of Wnt4 mRNA were higher in women with progressed endometriosis. The expression levels of Wnt4 were increased the progression of stage grouped by r-ASRM classification of endometriosis. Because r-ASRM classification is a gross classification, it may reflect progression of endometriosis genetically.

**Keywords:** Wnt4 endometriosis mRNA

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### SEMINAL PLASMA STIMULATES ENDOMETRIAL CYTOKINE PRODUCTION AND PROMOTES ENDOMETRIOSIS-LIKE LESION DEVELOPMENT

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**Objectives:** Seminal plasma (SP) contains signalling molecules that stimulate cytokine production in cervical cells (Sharkey et al., 2012) and enhance endometrial cell proliferation (Khan et al., 2010). We hypothesised that these signalling molecules promote pro-inflammatory cytokine production in endometrial tissues, thereby enhancing their ability to form endometriosis lesions at ectopic sites.

**Design:** We treated primary human endometrial fibroblasts (HEF; n=10) and tissue explants (n=4) with pooled SP (n=10) for 24h and assessed cytokine levels in conditioned media by ELISA and Luminex. The effect of SP on endometriosis-like lesions in vivo was assessed using the SCID mouse xenograft model (n=3-8/group in 4 experiments).

**Materials and Methods:** For in vivo studies, endometrial tissues were pre-incubated with 10% SP for 24h and/or mice were injected with 10% SP intraperitoneally. Endometriosis-like lesions were recovered, measured and weighed after 14 days.

**Results:** IP-10 and MCP1 were significantly up-regulated in primary HEF conditioned media after SP exposure ( $p < 0.05$ , paired T-test), while RANTES was significantly ( $P < 0.05$ ) down-regulated. In tissue explants, SP significantly ( $p < 0.05$ , 1-way ANOVA) increased GM-CSF, Gro, IL-1 $\beta$ , IL-10, MDC, and MIP-1 $\beta$  production. In mice, pre-incubation of endometrial tissue with SP resulted in endometriosis-like lesions that were 4.9-fold larger and 3.2-fold heavier ( $P < 0.05$ , Mann-Whitney U) compared to controls. Intraperitoneal exposure demonstrated a non-significant tendency toward increased lesion size and weight.

**Conclusion:** Although the applicability of these findings to human disease remains unknown, the data support the hypothesis that SP exposure favours the development of endometriotic lesions by promoting pro-inflammatory cytokine production in endometrial tissue. Studies are underway to determine the clinical relevance of this phenomenon.

**Keywords:** Seminal plasma, cytokines

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**DOES FEMALE GENITAL OBSTRUCTION CAUSE PELVIC ENDOMETRIOSIS?  
ANALYSIS OF HERLYN-WERNER-WUNDERLICH COMPLICATED WITH ENDOMETRIOSIS**

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**Objectives:** To explore the relationship between obstructive genital abnormality and pelvic endometriosis and clinical characteristics of these patients.

**Design:** Retrospectively review clinical charts of 94 cases of HWWS admitted in department of Obstet & Gynecol of Peking Union Medical College Hospital between 1995 to 2013. Median follow-up was 26.5 months.

**Materials and Methods:** Retrospectively review clinical charts of 94 cases of HWWS admitted in department of Obstet & Gynecol of Peking Union Medical College Hospital between 1995 to 2013. Median follow-up was 26.5 months.

**Results:** The incidence of pelvic endometriosis in HWWS was 19.15%(18/94) with mean age at diagnosis of EM was 17.8±5.35 years. There was a significant statistical difference compared with the mean age at diagnosis of HWWS(P=0.019). So do age at vaginal septum operation, the duration between time at EM diagnosis and menarche in complete and incomplete obstructed septum (P=0.03;P=0.025;P=0.025). 88.89% (16/18) endometriosis occurred before the diagnosis of HWWS and 94.44% ovarian endometrial cysts occurred ipsilaterally. EM recurrence rate was higher in cervical atresia cases than in those without cervical atresia or underdevelopment (71.4% vs 30%, P=0.059) while the EM recurrence rate was near same between incompleting and completed obstruction (50% vs 40%,P=0.671).

**Conclusion:** One of fifth patients of HWWS were liable to pelvic endometriosis, and almost all the ovarian EM cysts was ipsilateral to the vaginal septum. EM recurrence seem to have close relationship with cervical atresia in patients with HWWS.

**Keywords:** HWWS, pelvic endometriosis

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**EVALUATION OF EXPRESSION LEVELS OF NODAL AND CRIPTO IN EUTOPIC ENDOMETRIUM OF WOMEN WITH AND WITHOUT ENDOMETRIOSIS**

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**Objectives:** The aim of the present study was to evaluate the gene expression and the protein levels of Nodal and Cripto in endometriosis.

**Design:** It was transversal case control study.

**Materials and Methods:** Total RNA was isolated and cDNA synthesized from endometrium eutopic of women with (n=9) and without (n=6) endometriosis followed by quantitative real-time PCR (qPCR) to evaluate the gene expression of Nodal and Cripto. Western Blot was accomplished to evaluate the protein levels of Nodal and Cripto.

**Results:** Cripto gene expression was lower in eutopic endometrium of women with endometriosis than in controls (fold change 0.27 versus 1.0, p =0.03). No statistical differences were found in the gene expression of Nodal (fold change 1.0 versus 0.77, p >0.05). In relation to the protein levels of Nodal and Cripto, no alterations were found (relative density 1.0 versus 1.3, p>0.05 for Nodal; relative density 1.0 versus 1.02, p>0.05, for Cripto).

**Conclusion:** Cripto is known to be a co-receptor of Nodal, but once we found a decrease in gene expression of Cripto and no alterations Nodal expression were found, our results suggest that Cripto might be involved in the endometriosis pathogenesis in a Nodal-independent way.

**Keywords:** Nodal, Cripto, Endometriosis

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**IN VITRO ANALYSIS OF ENZYMES RELATED TO ESTROGEN METABOLISM EXPRESSION IN PRIMARY CULTURES IN THE ENDOMETRIUM OF PATIENTS WITH ENDOMETRIOSIS AFTER EXPOSURE TO PROGESTERONE**

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**Objectives:** Face of evidences that alterations in the cell cycle of the endometrium are involved in the pathogenesis of endometriosis, due to a dysfunction of this tissue to progesterone exposure, this study aims to evaluate the expression of aromatase (CYP19), sulfotransferase (SULT1E1), sulfatase (STS), StAR, 17beta HSD1, 2 and 4.

**Design:** Primary endometrium cell cultures of women with superficial and deep endometriosis, and control were treated with estrogen and progesterone.

**Materials and Methods:** After the treatment, the analysis of these enzymes expression was performed, through the techniques of quantitative PCR in real time, using as normalizing beta actin and cyclophilin A.

**Results:** After hormone treatment, we observed an increase about four times in the enzyme 17beta HSD1 expression, and twice in the aromatase (CYP19) of control patient's cells. In cases of superficial endometriosis, the expression of these same enzymes was inhibited. Also, sulfatase (STS) was slightly more expressed in the control and superficial endometriosis cells. However in cells from patients with deep endometriosis were not observed expression changes.

**Conclusion:** the inhibition of the enzyme CYP19 and 17beta HSD1 expression, at least in cases of superficial endometriosis, would affect opposing the spread of the disease.

**Keywords:** Endometrium, endometriosis, steroidogenesis

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### ANIMAL MODEL OF INDUCED ENDOMETRIOSIS USING THE RHESUS MACAQUE

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**Objectives:** The mechanisms related to the development of endometriosis are not well understood. Non-human primates have been identified as the most appropriate model to study this disease. We aimed to establish an animal model of induced endometriosis using rhesus macaques (*Macaca mulatta*) at the Caribbean Primate Research Center (CPRC).

**Design:** This study was reviewed and approved by institutional IACUC. Autotransplantation of menstrual tissue into the peritoneal cavity of female rhesus macaques was performed by laparoscopy to induce peritoneal endometriosis. A pelvic surgeon with experience in the management of endometriosis confirmed the visual diagnosis of the disease.

**Materials and Methods:** Seven female monkeys, aged between 7 and 10 years old, without previous surgery and no pelvic sonogram abnormalities were examined. Menstrual tissue was collected by uterine lavage, and then immediately deposited by laparoscopy onto the ovaries and uterine surfaces during three consecutive menstrual cycles.

**Results:** Five of seven animals completed three surgeries for induction. Two animals were induced with menstrual tissue at least once, however did not complete the procedures due to irregular ovulatory cycles or severe cervical stenosis which blocked the collection of tissue. One of the five animals developed a clear vesicle at the uterine site as early as after the second inoculation. During procedures, two animals presented with weight loss but they recovered after last inoculation. Laparoscopy was performed 24 months after the last inoculation in animals that completed all 3 procedures, and all animals developed endometriosis. The endometriotic lesions found in the rhesus macaque resembled those described in baboons and humans, and included adhesion bands, clear and white vesicles, deep infiltrating fibrotic nodules and red-raised nodules.

**Conclusion:** We were able to demonstrate that endometriosis can be experimentally induced in the rhesus macaque. This animal model may contribute to our understanding of the pathogenesis and early events leading to pelvic endometriosis.

**Keywords:** Endometriosis, rhesus macaques

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LOSS OF NERVE FIBERS IN THE OVIDUCT ISTHMUS IN THE PATHOGENESIS OF ENDOMETRIOSIS

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**Objectives:** To determine the presence of nerve fibers in the oviduct isthmus in women with endometriosis compared with women without endometriosis.

**Design:** A prospective analytical study in an academic training hospital.

**Materials and Methods:** Histological sections of the oviduct isthmus tissues from women undergoing hysterectomy for endometriosis (n=24) and other benign gynecologic diseases (n=24) were immunohistochemically stained for PGP 9.5, SP, NPY, and VIP to reveal all nerve fibers, sensory nerve fibers and sympathetic and parasympathetic nerve fibers.

**Results:** Nerve fibers stained with PGP9.5, VIP and NPY in the oviduct isthmus were all significantly decreased in women with endometriosis as compared with women without endometriosis (P<0.05). In women with endometriosis, reduced nerve fibers stained with PGP9.5 and SP in the serosal layer, NPY in the muscular and mucosal layers, and VIP in the mucosal layer of the oviduct isthmus were all associated with the severity of the disease (P<0.05).

**Conclusion:** These results suggest that decreased nerve fibers in the oviduct isthmus in women with endometriosis in comparison to women without may imply a role in the pathogenesis of endometriosis.

**Keywords:** Endometriosis, Nerve fibers

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### ENDOMETRIOSIS, TRAUMA AND STRESS: HIDDEN CONNECTIONS A STUDY OF PATHOGENESIS IN 100 PATIENTS WITH ENDOMETRIOSIS

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**Objectives:** Endometriosis cells are different to Endometrium- what causes this transformation? My objective was to isolate traumatic trigger events, identifying links between stress and endometriosis. While the majority of patients recover, 17% develop Post Traumatic Stress Disorder (PTSD) and further immunological and genetic disorders. This work envisages a new pathogenesis.

**Design:** Despite affecting 14% of women, little is known about endometriosis and it's deemed incurable by clinicians. My belief in an initial trauma as a trigger has been proven right. For patients, difficult situations are easier to write about than to discuss- the research involved 100 patients responding to a questionnaire.

**Materials and Methods:** I examined the following, 25 answers: circumstances of the pain with ratings, chronic bleeding and a timeline of the condition, with surgical events. I examined family and social life, psychological trauma (death, accidents, violence, recent hospital visits), professional stress, pre-existing conditions, anxiety and sleeping disorders, plus any family history of endometriosis.

**Results:** The ages of the respondents were distributed as follows: under 20 9% 20-30 20% 30-40 36% 40-50 23% over 50 12%. There is a link between age at the time of trauma and localization of endometriosis. One or more traumatic events or stress was found in 93% of cases. It seems the earlier the trauma the more severe the disease. The longer the secret is kept the more severe the disease. In addition, the condition is more severe if there is family history endometriosis. We find a combination of several traumatic events in 35% of cases. The research aims at bringing trauma into awareness in order to build resilience and heal through the resumption of dialogue.

**Conclusion:** An incurable disease? Why is endometriosis so persistent? Chronic stress affects immunity, genetic modulation, oxidative stress and inflammation. High Telomerase activity up expresses anti-apoptosis genes. Oxidative stress, from retrograde menstruation, increases cells survival. Proinflammatories, macrophages and mastocytes are overwhelmed. MMP-7 Metalloproteinase prevents apoptosis, NF-κB regulates inflammation, proliferation and apoptosis inhibition.

**Keywords:** Stress. Trauma. Pathogenesis

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**PATHOLOGY-SURGICAL-RADIOLOGICAL CORRELATION OF THE PELVIC SITES INVOLVED BY ENDOMETRIOSIS**

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**Objectives:** Retrospectively evaluate the capacity of magnetic resonance imaging of the pelvis in preoperative planning of deep pelvic endometriosis

**Design:** Retrospective study evaluating MRI exams and the surgical findings correlating them to the pathological results

**Materials and Methods:** A retrospective study was conducted with 30 patients who underwent MRI of the pelvis with a specific protocol for evaluation of endometriosis by clinical symptoms and were subsequently subjected to laparoscopy or laparotomy (VLP) with biopsies of sites of endometriosis with pathological examination (AP)

**Results:** The main sites affected by endometriosis were uterosacral ligaments (23,3%), periureteral region (16,1%), rectosigmoid (13,3%) and ovary (12,2%). The correlation between MRI and pathological examination was statistically significant for the sites vagina, rectosigmoid and periureteral region. Comparing MRI and VLP it was found a significant correlation for the same three sites and also for the uterine wall

**Conclusion:** According to the data obtained in this study, one can conclude that the sites most often affected is the data present in the literature. This study demonstrated that MRI exam is effective to show involvement by endometriosis in the sites vagina, rectosigmoid and periureteral region

**Keywords:** endometriosis, MRI, pathology

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### UMBILICUS ENDOMETRIOMA: CASE REPORT AND LITERATURE REVIEW.

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**Objectives:** Report a case of umbilical endometrioma and collect data in the literature about this uncommon condition.

**Design:** Case report and review of articles on umbilical endometriosis available in electronic databases, dating from the last 5 years.

**Materials and Methods:** Patient 41 years old, female, with history of laparoscopic and laparotomic surgeries, who complained of pelvic pain, umbilic node and navel bleeding during the menstrual period for 5 years. Evolved with increasing lesion and intraumbilical cyclical pain. The examination shows umbilical nodule with 2 cm, brownish, hardened and fixed.

**Results:** The patient underwent surgical excision of the belly button lesion, which extended into the aponeurosis and showed 7 cm in the largest diameter. The pathology analysis showed stromal and glandular endometriosis well differentiated in subcutaneous soft tissues, with free margins of endometrial tissue. Literature data show that umbilical endometriosis is an uncommon disease, representing 0.5 to 1% of cases of extraperitoneal endometriosis. In most cases occurs by implantation of endometrial cells during surgical procedures. Surgical treatment with complete excision of the lesion is the treatment of choice for this disorder, with low recurrence rates when the lesion is removed with margins free of disease.

**Conclusion:** The umbilical endometriosis is a rare condition, however can cause several symptoms that impair quality of life of patients and has differential diagnosis with primary malignant and metastatic lesions. The diagnosis is simple and the correct treatment provides improvement in symptoms and appearance of the umbilicus with low recurrence rates.

**Keywords:** Endometriosis, umbilical, cutaneous

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**RISK FACTORS FOR RECURRENCE AND PREGNANCY RATES AFTER LAPAROSCOPIC OVARIAN ENDOMETRIOMA TREATMENT**

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**Objectives:** The study was designed to analyze pre-operative clinical and surgical findings at enucleation of ovarian endometrioma with their impact on recurrence and pregnancy rates.

**Design:** This is a prospective observational cohort study.

**Materials and Methods:** 550 patients with histologically verified ovarian endometriomas operated on at the Department of Obstetrics and Gynecology, University Hospital Kiel, Germany between 1995 and 2004 were included. Pre-operative data, surgical findings and post-operative outcomes of 289 endometrioma cases were evaluated. The average follow-up was 12.9 years.

**Results:** Ovarian endometriomas recurred in 23.9%. Risk factors identified for recurrence of endometriomas were pre-operative pain ( $p = 0.013$ ), dysmenorrhea ( $p = 0.013$ ), larger cyst size ( $> 8$  cm), younger age ( $< 25$  years) and pre-operative cyst rupture. Factors associated with post-operative dysmenorrhea were younger age  $< 25$  years ( $p < 0.001$ ), nulliparity ( $p = 0.020$ ) and larger cyst size  $> 8$  cm ( $p = 0.048$ ). Recurrence of pain was influenced by previous surgery of endometrioma ( $p < 0.05$ ). Laparoscopy had a higher percentage of symptom-free patients than laparotomy (49.0% vs. 33.3%). Additional post-operative hormonal treatment resulted in a higher spontaneous pregnancy rate (41.4% vs. 12.6%;  $p < 0.001$ ) and a lower recurrence-free interval rate (70.5% vs. 82.6%;  $p = 0.050$ ) when compared to surgery only.

**Conclusion:** We identified pre-operative and intra-operative findings associated with higher risk of recurrence of endometrioma, pain and dysmenorrhea. These results suggest that patients desiring pregnancy benefit from post-operative hormone treatment; however no favorable results from combined therapy were observed with regard to recurrence rate.

**Keywords:** Endometrioma, recurrence

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PELVIC ENDOMETRIOSIS IN WOMEN UNDER 25: A SPECIFIC MANAGEMENT ?

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**Objectives:** To study the characteristics of women under 25 years with pelvic endometriosis and assess their potential for recurrence and fertility after surgery.

**Design:** Comparative retrospective study. 88 patients aged less than 25 years were included: 42 in the DIE group (deep infiltrating endometriosis) and 46 in the SE group (superficial endometriosis).

**Materials and Methods:** The criteria considered were patient characteristics, the results of imaging studies, previous surgery and postoperative treatments, the symptoms, the type of surgical procedure and the postoperative follow-up (postoperative complications, recurrences, subsequent fertility).

**Results:** The diagnosis was made at  $21.6 \pm 2.8$  years, mainly considering clinical signs (78.4%), and on average  $4.3 \pm 3.7$  years after the onset of symptoms. 16.1% of patients had to be reoperated (n=5/31) due to a recurrence of their endometriosis. There were more recurrent pain (50% vs. 21.7%, p=0.005) and endometriosis (35.7 vs. 19.6%, p=0.08) in the DIE group. 75% (n=33/44) patients desired pregnancy after surgery and 50% of them became pregnant, with one third thanks to Assisted reproductive technology.

**Conclusion:** In young women, endometriosis is often more severe. The early treatment does not improve the rate of recurrence and fertility, but can reduce pain and thus improve the quality of life.

**Keywords:** Teenager; Fertility; Recurrence

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**PREVIOUS HISTORY OF SURGERY FOR ENDOMETRIOSIS IS A MARKER FOR PRESENCE AND SEVERITY OF DEEP INFILTRATING ENDOMETRIOSIS**

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**Objectives:** Endometriosis has a high risk of recurrence, which often leads to multiple surgical procedures for patients. However, little is known regarding the characteristics of patients receiving previous surgery for endometriosis. Does a previous history of surgery for endometriosis serve as a marker for disease severity?

**Design:** This cross-sectional study included 780 women with histologically proven endometriosis who underwent surgery between January 2003 and August 2012. We compared 309 patients with a previous history of surgery for endometriosis (study group) to 471 patients who did not receive prior surgical intervention (control group).

**Materials and Methods:** For each patient demographics and medical characteristics prospectively collected, including their adolescent history. According to surgical findings, the patients were classified based on the following criteria: histological grade (i.e., superficial endometriosis [SUP], ovarian endometrioma [OMA], and deep infiltrating endometriosis [DIE]) and number and location of DIE lesions.

**Results:** Patients with a previous history of surgery displayed an increased prevalence of DIE as compared with the control group (242[78.3%] vs. 210[44.6%], respectively;  $p < 0.001$ ). Furthermore, history of previous surgery remained independently associated with the presence of DIE in multivariate regression analysis, which adjusted for preoperative pain scores, age, body mass index, smoking habits, oral contraceptive use, infertility, and parity (aOR=2.96, 95% CI=1.99–4.39;  $p < 0.0001$ ). The number of previous surgeries for endometriosis correlated significantly with lesion severity. Finally, among women presenting with DIE ( $n=452$ ), previous surgical history was significantly associated with a higher mean number of DIE lesions ( $3.1 \pm 1.9$  vs.  $2.6 \pm 1.8$ ;  $p=0.001$ ) and with increased severity of DIE lesions, especially in the case of intestinal lesions (159[66.0%] vs. 77 [37%],  $p < 0.001$ ).

**Conclusion:** Prior surgical history for endometriosis is a marker for both the presence and severity of deep infiltrating endometriosis (DIE).

**Keywords:** Deep-infiltrating-endometriosis, endometriosis, previous-surgery

Poster - Prevention and management of recurrences

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**POSTOPERATIVE RECURRENCE FACTORS OF FUNCTION-SPARING SURGERY FOR ENDOMETRIOMA AND DEEP INFILTRATING ENDOMETRIOSIS (DIE) AND WELL-TIMED HORMONAL THERAPY**

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**Objectives:** Because of increasing numbers of endometriosis patients want to preserve fertility, new strategies for function-sparing surgical treatment are required. To identify recurrence factors, we retrospectively reviewed recurrence rates after function-sparing surgery for endometrioma and DIE as well as the effects of post-operative prophylactic hormonal therapy and well-timed intervention.

**Design:** A retrospective non-randomized open-label study

**Materials and Methods:** 157 women who had undergone function-sparing surgery for endometrioma or DIE between 2005 and 2013 with a minimum follow-up of six months were reviewed and classified into a non-recurrence group, a symptom recurrence group, and a lesion recurrence group. Recurrence rates after surgery were examined by the Kaplan-Meier method.

**Results:** The average age of the patients was  $32.9 \pm 6.3$  years. The total cumulative recurrence rate of endometriosis after surgery was 30.0%, while lesion recurrence rate was 16.3% according to the Kaplan-Meier method. In the recurrence group, age was significantly lower ( $33.5 \pm 6.4$  years of age vs.  $30.3 \pm 5.7$  years in the non-recurrence group) and r-ASRM score was significantly higher ( $48.3 \pm 33.1$  vs.  $66.6 \pm 29.0$ ). No association was observed between recurrence rate and prophylactic hormonal therapy after surgery. Of the 16 patients in the lesion recurrence group, seven required a second surgery, while nine avoided additional surgery through early intervention with hormonal treatment. All 18 cases in the symptom recurrence group were controlled through conservative therapy, avoiding additional surgery.

**Conclusion:** Well-timed intervention with hormonal therapy after function-sparing surgery for endometrioma and DIE can suppress the recurrence of lesions and help patients avoid additional surgery.

**Keywords:** Function-sparing surgery

## Poster - Quality of life

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### CURRENT TRENDS IN THE STUDY OF QUALITY OF LIFE IN ENDOMETRIOSIS PATIENTS

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**Objectives:** To analyze from PUB MED databases a series of articles dedicated to investigate QOL of endometriosis patients in the time lapse October 2006 / October 2013 and describe the questionnaires used, the number of treated patients and other notable characteristics of those essays. No statistical endpoints were searched for.

**Design:** Literature review using PUB MED database and descriptive analysis of the search results.

**Materials and Methods:** Twenty-six qualified articles, in a large range of study designs, representing investigations from 13 countries, making the sample interesting due to its universality. A simple non statistical mathematical and non-mathematical analysis of the articles, to best describe the current trends prevailing today related to the study of endometriosis patients' QOL.

**Results:** : The 23 studies that surveyed patients included a total of 4872; SF36: 2755 individuals, EHP 30 surveys: 1474, EHP5: 18, (WERF) GSWH: 931, 15D Questionnaire and McCoy Female Sexuality Questionnaire: 48, pain 10-point visual analog scale: 220, self-constructed questionnaires: 170, the general health version of the Work Productivity and Activity Impairment (WPAI:GH) for absentism and presentism: 1418, the World Health Organization Quality of Life Assessment-Brief (WHOQOL-BREF) quality of life questionnaire: 48, the same presentation added the Golombok-Rust Inventory of Sexual Satisfaction (GRISS) in their survey, Patient Reported Outcome (PRO) forms: 108, and finally, the Sexual Satisfaction Subscale of the Derogatis Sexual Functioning Inventory: 98. The analytical reviews addressed a large number of different QOL surveys.

**Conclusion:** : The SF36 is the most widely employed questionnaire (in number of patients reported), the EHP 30 second with 1474 individuals, the WPAI: GH third with 1418, and the (WERF) GSWH fourth with 931. Shorter forms should be favored looking at the rate of response, and endometriosis specific questionnaires prioritized.

**Keywords:** endometriosis, QOL, questionnaires

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### DEVELOPMENT OF A FRENCH VERSION OF THE ENDOMETRIOSIS HEALTH PROFILE (EHP-5): CROSS-CULTURAL ADAPTATION AND COMPARISON WITH THE EQ-5D

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**Objectives:** The Endometriosis Health Profile (EHP-5) is a short version of the endometriosis specific quality of life assessment questionnaire. An adaptation of this questionnaire was developed in French. Our study concerns its psychometric validation, comparing its results with those of a general questionnaire of quality of life: the EQ-5D.

**Design:** Cross-sectional quantitative study of patients operated for painful endometriosis and asymptomatic control women recruited from the medical staff in two French tertiary referral centers.

**Materials and Methods:** 125 patients with histologically-proven endometriosis and 80 asymptomatic controls completed the EHP-5 and the EQ-5D. Principal components analysis was performed to determine the dimensions of the instrument and to assess its internal consistency. Construct validity was assessed by testing the relationship between EHP-5, EQ-5D and endometriosis characteristics.

**Results:** The 11 items of the EHP-5 were unidimensional according to principal component analysis. Internal consistency of EHP-5 was excellent (Cronbach alpha= 0.92). EHP-5 and EQ-5D were both sensitive to the presence of endometriosis, to the type, location, severity of the disease, and pain or infertility as a main complaint. Effect sizes were nonetheless significantly larger for EHP-5 and ranged from 0.41 (95%CI = 0.04-0.78) to 2.47 (95%CI = 2.10 - 2.85) for EHP-5 and from 0.17 (95%CI = -0.12 - 0.45) to 1.48 (95%CI = 1.16 - 1.79 for EQ-5D).

**Conclusion:** The French version of EHP-5 is valid and its comparison to the EQ-5D revealed that the EHP-5 was more sensitive to the characteristics of the disease than the EQ-5D. EHP-5 should represent a valuable tool for reporting patient-orientated outcome in future studies of French-speaking patients with endometriosis.

**Keywords:** Endometriosis/Quality of life/questionnaire

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### THE RELATIONSHIP BETWEEN QUALITY OF LIFE AND CATASTROPHIC THOUGHTS IN WOMEN WITH ENDOMETRIOSIS TREATED IN A PAIN MANAGEMENT CENTER IN BRAZIL

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**Objectives:** To compare the quality of life domains in patients with and without catastrophic thoughts, in their first visit to a private Pain Management Center, in Sao Paulo.

**Design:** This is a cross sectional study conducted with 22 patients with endometriosis and chronic pelvic pain (for over 6 months), evaluated from July 2012 to July 2013

**Materials and Methods:** The Pain Catastrophizing Scale was applied in all patients with endometriosis at their first visit to a Pain Management Center. The following data was also analyzed: age, pain assessment according to the numerical verbal scale (NVS), scores of SF- 36 a quality of life measure were also assessed.

**Results:** The mean age of the sample was 35. Based on a Numerical Verbal Scale to assess pain intensity, 28% of the patients referred moderate pain and 72% strong pain in the first visit. 10 patients (46%) presented positive catastrophic thinking in The Pain Catastrophizing Scale. Scores of the SF-36 were compared between patients with and without catastrophic thoughts. Significant differences were found between groups ( $p=0.01$ ). As described below patients with catastrophic thoughts had lower scores in all the dimensions of the SF-36. 80% and 27% in the physical functioning, 70% and 0% in the social functioning, 80% and 27% in vitality, 80% and 18% in the emotional dimension, 60% and 18% in the mental health domain, and 60% and 36% in physical domain.

**Conclusion:** Patients with positive catastrophic thoughts have greater impact in quality of life as compared to those individuals not presenting catastrophic thoughts. Evaluating catastrophic beliefs showed to be a relevant initial approach for patients with endometriosis and moderate-to-severe chronic pelvic pain. Better multidisciplinary treatment can be proposed based on these scales.

**Keywords:** pain, endometriosis, catastrophizing

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### IMPACT ON QUALITY OF LIFE OF LAPAROSCOPIC COLORECTAL SEGMENTAL RESECTION IN WOMEN WITH DEEP ENDOMETRIOSIS

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**Objectives:** To aim of this study was to evaluate the changes in quality of life over 6 months and one year follow-up period in patients submitted to laparoscopic bowel segmental resection for the treatment of deep endometriosis.

**Design:** We have designed a prospective study analyzing 295 women with deep bowel infiltrating endometriosis submitted to laparoscopic segmental bowel resection regarding quality of life after surgery.

**Materials and Methods:** From July 2009 and Setember 2012, 295 women diagnosed by transvaginal ultrasound with bowel preparation with endometriosis intestinal involvement compromising the muscularis were submitted to a colorectal resection. The subjects completed the World Health Organization Quality of Life Assessment-Bref quality of life questionnaire pre-operatively, 6 months and 1 year post-operatively.

**Results:** The physical functioning, role physical, social functioning and role emotional subscales evidenced the most important median increases for T0, 6 months and 1 year. Significant improvements were observed in all domains of the SF-36 throughout the study period ( $p < 0.05$ ). Physical health-related QOL domains showed greater improvement than mental health. Regarding to age, parity and body mass index as potential factors influencing the impact of surgery on QOL showed no differences. However these factors were not used as prognostic indicators for the surgical procedure or for patient follow-up. In addition, we noted that the patients with the poorest results on the initial QOL questionnaire showed the greatest improvements after one year.

**Conclusion:** The study results showed that laparoscopic segmental colorectal resection for endometriosis had a positive impact on quality of life. We could also observe that these effects persisted also 1 year after surgery

**Keywords:** QOL, laparoscopy, endometriosis

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### THE EFFECTS OF ETONOGESTREL SUBDERMIC IMPLANT (IMPLANON®) IN DYSMENORRHEA, ABNORMAL UTERINE BLEEDING AND ESTRADIOL SERUM IN PATIENTS WITH PELVIC ENDOMETRIOSIS.

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**Objectives:** Evaluate the effects of etonogestrel subdermic implant (Implanon®) in dysmenorrhea, abnormal uterine bleeding and estradiol serum level in patients with pelvic endometriosis.

**Design:** The effects of the medication on dysmenorrhea and uterine bleeding were analyzed with 0, 3, 6, 12, 24 and 36 months of treatment, what causes treatment discontinuation with this medication and the levels of estradiol serum.

**Materials and Methods:** Were analyzed 41 patients were diagnosed through surgical videolaparoscopy with pelvic endometriosis (Group 1) using subdermic implant containing 68 mg of etonogestrel (Implanon®), and compared to 35 patients using the implant only as contraceptive method (Group 2).

**Results:** After 36 months of treatment, in group 1, abnormal uterine bleeding appeared in 6 of 31 patients that were still using the implant (19.4%), compared with 3 of 16 from Group 2 (18.8%) using the same criteria. Regarding dysmenorrhea, all patients from group 1 presented pain at the beginning of the treatment, and by the end of 36 months of treatment, 29 from 31(93.5%) patients claimed pain reduction. In group 2, all the 16 patients presented pain reduction (100%). The implant extraction with less than 36 months of treatment happened with 10 patients (24.4%), and in group 2, 9 users removed the implant before the completion of treatment (25.7%). The evolution of estradiol serum was similar in both cases throughout the duration of 36 months.

**Conclusion:** The etonogestrel subdermic implant hormonal treatment in patients with pelvic endometriosis managed to reduce pelvic pain, the abnormal bleeding patterns didn't show as a significant collateral effect when compared to the use of the implant as a contraceptive method, representing a suitable alternative for pelvic pain control.

**Keywords:** Dysmenorrhea, etonogestrel implant

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### IMPACT OF LAPAROSCOPY ON THE QUALITY OF LIFE OF WOMEN WITH DEEP ENDOMETRIOSIS - LONG TERM FOLLOW UP

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**Objectives:** To evaluate the long term impact of surgical laparoscopic treatment on quality of life in women with deep infiltrative endometriosis

**Design:** A prospective observational cohort study was conducted. (Canadian Task Force Design Classification II)

**Materials and Methods:** Forty patients submitted to laparoscopy for deep endometriosis was selected to answer the SF-36 questionnaire before the surgery, 12 and 48 months after the surgery and compared the different items of the SF-36 on the different times of application. Statistical analysis was performed with test of variance analysis (ANOVA).

**Results:** During the study period, a total of 36 patients answered the questionnaire in the 3 different moments. After analysis of each domain, observed an improvement on quality of life when compared the period before surgery with 12 and 48 months after surgery. There was a significant increase ( $p < 0,001$ ) in scores in all the SF-36 domains when compared T0 x T12 and T0 x T48. Physical functioning presented average values (T0-33,90/ T12-93,19/ T48-85,56) higher than mental health (T0-37/ T12-66,22/ T48-67,08).

**Conclusion:** The laparoscopic treatment for deep infiltrative endometriosis improve the quality of life in a long term.

**Keywords:** Endometriosis, laparoscopy, quality

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### DEVELOPMENT AND ASSESSMENT OF A WEB-BASED SOFTWARE APPLICATION TO FACILITATE SELF-EDUCATION AND SYMPTOM DOCUMENTATION IN WOMEN UNDERGOING SURGERY OR MEDICAL THERAPY FOR ENDOMETRIOSIS

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**Objectives:** Our objective is to create a web-based application that facilitates the administration of pain and quality of life surveys for patients with endometriosis. By digitalizing the surveys, our goal is to streamline data collection and increase the accuracy of symptom documentation.

**Design:** We created a web-based educational and symptom survey tool which is easily accessible on most internet-capable devices including smartphones and tablets. A novel software program, Mylar, encrypts patient responses to questionnaires and stores the encrypted data in a secure data repository, accessible only to patients and investigators.

**Materials and Methods:** Our application is a product of the collaborative efforts of a multi-disciplinary group from MIT and Newton-Wellesley Hospital, including gynecopathology researchers, individuals with endometriosis, security software engineers, and clinicians. It is formatted with expandable tabs and one-touch responses, making the application easily navigable via smartphones and tablets.

**Results:** We created a user-friendly application, usable on most personal digital devices that quickly and efficiently documents symptoms related to endometriosis. The application relays important educational information from the physician to the patient. It prompts patients to perform self-evaluations, triggering messages to call in for alarming symptoms. For investigators, the Mylar software allows easy, secure passage of information from patients in real time via weekly questionnaires. The interface is easily modifiable, allowing investigators to adjust data points and informational content quickly, with immediate upload onto the application. After implementation with our patients, we will report results of subject satisfaction surveys, subject adherence, and evaluations from collaborators.

**Conclusion:** We have created a digital, secure application for data collection, which will increase the accuracy of endometriosis symptom documentation and facilitate exchange of information between clinicians and patients. Our model will have wide ranging applicability to investigators interested in documenting endometriosis symptoms and outcomes of various therapies.

**Keywords:** Mylar, Endometriosis, Survey

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### COMPARISON BETWEEN PHYSICAL ACTIVITY AEROBIC AND ANAEROBIC IN EXPERIMENTAL ENDOMETRIOSIS

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**Objectives:** The objective of this study was to compare the therapeutic response of aerobic and anaerobic activities in reducing endometrial implants in experimental rats

**Design:** This study characterizes methodologically as experimental and that the experiments were performed following the ethical standards and principles of the Brazilian College of Animal Experimentation (COBEA) and with the approval of the Bioethics Ethics Committee on the use of animals.

**Materials and Methods:** Forty wistar rats were submitted to induction of peritoneal endometriosis. After 21 days, there were reopening to confirm the disease and establish protocols. After 48hours, were divided into 4 groups: control, aerobic activity, anaerobic activity and mixed activity 3 times a week for 2 months.

**Results:** Of the rats underwent anaerobic activity (n = 8), 12.5% implantation increased 37.5% remained unchanged and 50% decreased. Those who performed aerobic activity (n = 9) the results were similar, increased 11.1%, 33.3% and 55.5% remained the same decreased. The mixed activity showed an increase in 44.4% of rats, decreased 44.4% and 11.1% remained the same. The rats in the control group (n = 10), 80% of the implants increased and 20% decreased.

**Conclusion:** The study concludes that physical exercise can reduce the implants, with no significant difference between aerobic and anaerobic activities.

**Keywords:** Physical activity, endometriosis

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### SEXUAL ASPECTS IN WOMEN WITH ENDOMETRIOSIS: PRELIMINARY RESULTS

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**Objectives:** The aim of this study is to identify the presence of sexual dysfunction in women with endometriosis and compare it to patients without the disease. Specific evaluations will be performed concerning the different types and stages of endometriosis, clinical symptoms, presence of anxiety, depression and correlated diseases .

**Design:** A prospective randomized analytical study

**Materials and Methods:** 508 women will be equally distributed in two groups and will answer three questionnaires: Female Sexual Quotient (FSQ), Beck Anxiety and Beck Depression Inventory (IRB Approval 248.015). Respective sexual partners will answer the Male Sexual Quocient. Patients with severe depression or anxiety or dysfunctional relationship will be excluded.

**Results:** From March to September 2013, we interviewed 216 patients (141 with endometriosis and 75 controls). The rate of global depression was 33.3% (47/141) in endometriosis group, while severe depression was found in 16.3% of them versus 28% (21/75) in control group. Anxiety was found in 49.6% (70/141) endometriosis group versus 46% (35/75) in control group but severe anxiety corresponded to 26.2% of patients with endometriosis. 14.8% of sexual partners have answered the questionnaire of endometriosis group and 12% of control group. Mean Quotient Sexual Female scores were, respectively, 59.87 and 68.08 for endometriosis patients and control patients showing an unfavorable/regular sexual score pattern in the case group and a favorable/good pattern in the control group, according to the evaluation of FSQ original questionnaire.

**Conclusion:** Even though the presence of Endometriosis itself may worsen sexual performance, the highest factors of impairment are due to the coexistence of severe anxiety and depression besides Endometriosis, so these conditions must be treated to improve hole medical assistance and global quality of life for these patients.

**Keywords:** Endometriosis, Sexual Dysfunction

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### EVALUATION OF NURSE-LED EDUCATION FOR WOMEN WITH ENDOMETRIOSIS AND PELVIC PAIN

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**Objectives:** Therapeutic patient education is known to be effective in some illnesses. The aim of this study was to evaluate the effectiveness of nurse-led education on women's knowledge and management of endometriosis and pelvic pain.

**Design:** Mixed method design including quantitative tools: SF-12 (12 item Short-Form Health Survey), the Brief Pain Inventory short form (BPI-sf) and the Pain Stages of Change Questionnaire (PSOCQ); and semi structured telephone interview 4-8 weeks post visit.

**Materials and Methods:** Women referred for endometriosis and/or pelvic pain were eligible for the study. After consent, online links were sent for pre and post (4 weeks after visit) questionnaires. The structured visits included health assessment, education, tailored management and health planning. Phone interviews were conducted after post questionnaires were completed.

**Results:** 37 women completed questionnaires pre-visit. 37 visits occurred. 16 women completed the post-visit questionnaire and 15 were interviewed by phone. Age range: 17-44 (Mean =29.37, SD = 7.75). 31% had laparoscopic diagnosis of endometriosis. Women who initially reported their level of information to be medium or lower, reported increases in their knowledge level (10/14). 11/15 women reported new or different actions or thinking about endometriosis post education session. 10/15 women reported using lifestyle measures after the session. Analysis of data from the tools is ongoing. Thematic analysis of phone interviews produced three global themes: 1. Experience of the education session (1.1 Getting information 1.2 Learning self-management 1.3 Personalised care; 1.4 Breaking isolation) 2. What would help and 3. Struggles associated with living with endometriosis.

**Conclusion:** Nurse-led screening and education increased women's health knowledge and adoption of self-management practice. Given current limited treatment options, nurse-led education provides an extra component of therapy that may assist women with managing the daily manifestations of endometriosis and ongoing pelvic pain. Future research should examine long term sustainability and outcomes.

**Keywords:** Endometriosis, education, nurse-led

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### ASSESSMENT OF HISTOLOGICAL CLASSIFICATION AND QUALITY OF LIFE IN WOMEN WITH ENDOMETRIOSIS.

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**Objectives:** To assess the histological classification and quality of life in patients operated for endometriosis.

**Design:** An observational, cross-sectional pilot study was conducted.

**Materials and Methods:** A total of 32 biopsies: intestine, peritoneum and uterosacral ligament in 40/women with deep endometriosis stage IV. Quality of life was evaluated applying SF-36/questionnaire pre-operatively during 6/12 months post-operatively. Biopsies were classified into pure stromal and glandular: differentiated, undifferentiated, mixed. Histological types for each site were related to 8 domains SF-36.

**Results:** Biopsy finding in peritoneum were: 7% pure/stromal(PS), 10% glandular/differentiated(DG), 63% undifferentiated(UG) and 22% mixed(MG); Intestine: absence of PS, 7%DG, 19%UG 24%MG; Uterosacral ligament: 13%PS, 10%DG, 41%UG, 35%MG. Regarding Quality of life(QoL) and histological classification, evolution of intestine: MG was associated with improvement from 0/6 months social and emotional aspects. Peritoneum: UG showed health status ( $p=0.010^*$ ) and social aspect ( $p=0.04^*$ ) had significant relationship with improvement QoL from 0/6 months; and tendency in health status from 0/12 months. Pain ( $p=0.066$ ) emotional aspect ( $p=0.055$ ) showed tendency for improvement QoL from 0/6 months and vital capacity ( $p=0.110$ ) for follow-ups 0/6 and 0/12 months. Emotional aspect, evolution of the two histological types was not favorable for improvement in MG from 0/6 months. No significant relationships were evident the uterosacral ligament.

**Conclusion:** UG in the peritoneum was associated with significant improvement in QoL for the domains 4 and 6, and a tendency for improvement for domains 1, 3 and 7, post-operatively. For the other domains and sites, no influence of histological classification on QoL was evident.

**Keywords:** Histology, Quality life

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### LIVING AND MANAGING LIFE WITH ENDOMETRIOSIS: RESOURCES FOR TEENS AND THEIR FAMILIES

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**Objectives:** The Center for Young Women's Health at Boston Children's Hospital is an educational entity that develops, implements, and disseminates carefully researched health resources and initiatives. The objective of this initiative was to improve the quality of life for teens diagnosed with endometriosis and their families.

**Design:** We polled a group of young women to identify resources that would improve their quality of life with endometriosis. We applied and received funding to create resources based on feedback. Moderated online support chats, educational resource booklets, and an annual conference for teens and their families were created.

**Materials and Methods:** Endometriosis causes debilitating pelvic pain and infertility. Fifty percent of adult women with endometriosis have symptoms prior to age 22, yet it is not well recognized as a disease that affects teens. Documented rates of endometriosis in adolescent patients (undergoing laparoscopy for chronic pelvic pain) range from 19% to 73%.

**Results:** 1. Free, moderated monthly online chats for teens with endometriosis. 2. Publication and dissemination of "Preparing for your Laparoscopy", "Managing Your Life with Endometriosis" and, "Helping Your Daughter Manage Endometriosis" resource booklets. 3. An annual conference for teens and their families, including a keynote lecture on new developments, treatment, and fertility, support groups, workshops on osteopathic manipulative therapy, healthy eating, acupuncture, and yoga, and a question and answer health panel with faculty. 4. A free, live webcast of the keynote and a re-broadcasted recording. 5. Collection and analysis of conference assessment data obtained from participants.

**Conclusion:** Since the inception of the initiative, we've received feedback from 160+ families. Evaluations assess overall satisfaction, and we've learned that teens and families are overwhelmingly appreciative of the opportunity to learn more about endometriosis, ways to cope with chronic pain, and to meet others with whom they can identify.

**Keywords:** Endometriosis, online chats

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### ENDOMETRIOSIS PATIENTS IN THE POSTMENOPAUSAL PERIOD: PRE- AND POSTMENOPAUSAL FACTORS INFLUENCING POSTMENOPAUSAL HEALTH

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**Objectives:** To evaluate patients' health status and the course of endometriosis from the premenopausal to the postmenopausal period and evaluate influencing factors that may be relevant.

**Design:** Questionnaire in an endometriosis competence center.

**Materials and Methods:** Questionnaire completed by 35 postmenopausal women in whom endometriosis had been histologically confirmed premenopausally. Correlation analyses were carried out to identify factors relevant to their postmenopausal health status.

**Results:** Overall, there was clear improvement in typical endometriosis symptoms and sexual life. Clear associations ( $p < 0.005$ ) were observed between premenopausal factors like physical limitations caused by the disease, impaired social contacts and psychological problems, and postmenopausal pain and impairment of sexual life. All forms of medication including their duration and alternative therapies, pregnancy and parity proved to be quite unimportant influencing factors relative to the postmenopausal target variables mentioned. The number, type and method (surgical techniques) of operations carried out also hardly correlated at all with the target variables "general pain experienced," "pain during sexual intercourse," and "disturbance of sexual life".

**Conclusion:** This study strongly suggests that physical fitness and freedom from physical symptoms, a good social environment, and psychological care in both the premenopausal and postmenopausal periods lead to marked improvements in the postmenopausal period with regard to pain, dyspareunia, and influence on sexual life in endometriosis patients.

**Keywords:** Endometriosis; postmenopause

## Poster - Quality of life

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### UNDERSTANDING WOMEN'S EXPERIENCES OF ENDOMETRIOSIS AND OF CONDITION-SPECIFIC HEALTHCARE

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**Objectives:** Patients' reported experiences of illness can highlight opportunities for improvement in clinical practice and health policy. Little is known about women's experiences of, and preferences for, the health care they receive for endometriosis. This study aimed to explore women's experiences of endometriosis and associated health care.

**Design:** A qualitative, interview-based study. Purposive sampling was used to enable inclusion of diverse experiences.

**Materials and Methods:** In-depths interviews were conducted with women aged at least 18 years who live in Victoria, Australia, who had been surgically diagnosed with endometriosis. Interviews were audio-recorded, transcribed, and analysed using Interpretative Phenomenological Analysis.

**Results:** Participants gave accounts of varied experiences of and attitudes to endometriosis-related health care. Women appreciated unhurried consultation, being listened to, and open-ended inquiries about the impact of illness on all areas of their life. Health professionals who demonstrated a commitment to care and developed a long-term management plan in conjunction with the woman were valued. Women were less satisfied with suggestions that the illness was psychogenic, that the condition could be managed by positive thinking, and being dismissed as intractable.

**Conclusion:** Women's accounts of their experiences of endometriosis revealed both the wide-ranging impact of this condition as well as areas of improvement for current clinical practice and public health policy. Such improvements may assist women and their health care providers to manage this complex condition.

**Keywords:** Endometriosis, qualitative, experience

## Poster - Quality of life

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### THE PERCEPTION OF ENDOMETRIOSIS IN DUTCH WOMEN

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**Objectives:** The goal of this study was to identify patients' perception of the way towards diagnosis of endometriosis.

**Design:** A questionnaire was sent to the members of the Dutch Endometriosis Society (ES). The results of this questionnaire were interpreted and points of attention for the ES were identified.

**Materials and Methods:** A descriptive study was conducted among members of the ES who had an email address (n=839). They received a questionnaire consisting of 62 multiple choice questions via email using Pontifexsurvey.nl, a commercial data processing company. Statistics were calculated using Excel for Windows.

**Results:** 349 (42%) women responded to the questionnaire. 13 women were excluded. Age at onset of complaints was 16.7 yrs (SD 6.4). The most important complaints were abdominal pain (90%), back pain (38%) and dyschezia (32%), influencing specifically social (68%) and professional (68%) life, and sexuality (43%). They visited their GP after 5.3 years (SD 6.8) of complaints. Perception was rated from unpleasant, neutral or pleasant (score 1, 2, 3 respectively) for the following items: first visit (1=26%, 2=46%, 3=28%); initial treatment (1=50%, 2=24%, 3=26%); general satisfaction with GP (1=24%, 2=26%, 3=50%). Women were most satisfied with their GP after referral (score 2.5) ( $p < 0.001$ ), as compared to hormonal treatment (score 1.7), pain treatment (score 1.3) and lifestyle advises (score 1.2).

**Conclusion:** Patients' delay before the diagnosis of endometriosis is long. The general satisfaction of patients with their GP is positive, although perception of the initial endometriosis care is poor. The ES aims at earlier recognition of complaints by young women themselves, in order to shorten patients' delay.

**Keywords:** Patient, Perception, Diagnosis

## Poster - Quality of life

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### EVALUATION OF HYPOESTROGENISM EFFECTS IN VAGINAL DISTENSION OF WISTAR RATS

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**Objectives:** Correlacionate estrogen levels and distension in rats` vaginal tissue.

**Design:** This is an experimental, prospective and controlled trial that studied the impact of the simulation of delivery and oophorectomy on the estrogen levels in rats` vaginal tissue.

**Materials and Methods:** Sixty wistar rats were divided into: "a" control group, "b" oophorectomized, "c" underwent vaginal distension for thirty minutes, "e" uderwent distention for one hundred and twenty minutes, "d" and "f" were group "c" and "e" ooforectomized. The hormonal analysis used touma and palme method and the data were statistically analyzed.

**Results:** Results: Statistical difference in estrogen levels were found in the comparison of ovariectomized x non ovariectomized rats ( $p < 0.0002$ ). However, in the multiple comparison study the differences between the control group x ovariectomized control; 30 minute vaginal distension x 30 minute vaginal distension plus ovariectomy, no statistical significance was found ( $p = 0.8405$  and  $0.1568$ , respectively).

**Conclusion:** The reduced concentration of estrogen in rats` vaginal tissue and castration was greater than that caused by distension plus castration, what may contribute with pelvic organs prolapses, whereas estrogen is deeply associated with the repair of tissues.

**Keywords:** Estrogen, vagina, oophorectomy

## Poster - Quality of life

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### LONG-TERM EVALUATION OF CLINICAL RESULTS , QUALITY OF LIFE, DIGESTIVE, SEXUAL AND URINARY SYMPTOMS AFTER SURGERY FOR DEEPLY INFILTRATING PELVIC ENDOMETRIOSIS.

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**Objectives:** Surgery for deep endometriosis with rectal muscularis involvement is difficult and controversial. We use a shaving method whenever possible. Bowel resection is used only if shaving is impossible. The present study was undertaken to assess long term clinical follow up after our surgical approach.

**Design:** Retrospective monocentric quality study using the following questionnaire : the Short Form 36 questionnaire, visual analog scale of pain, specific questions on sexual and digestive symptoms, ditrovie scale

**Materials and Methods:** 328 patients operated for an infiltrating nodule of more than 2 centimeters in diameter, with rectal muscularis involvement were included from January 2000 to June 2013, at the Hospital of Clermont-Ferrand. A questionnaire with validated research tools was sent to each patient to assess their symptoms and quality of life.

**Results:** Of these patients, 298 were treated by shaving and 30 underwent a bowel resection. Preoperative patient characteristics, rectal nodule features, major intraoperative and postoperative complications were collected retrospectively.. The mean age of patient in the shaving group was 32 years (range 15 to 50). The mean length of hospital stay was 4 days (SD : 2.58). The average overall duration of follow-up was 51months (range 1 to 214). Postoperative complications for shaving occurred in 30 patients, including 21 minor (7% ) and 7 major (3%) complications. In segmental resection, minor postoperative complications developed in 4%, and major in 1,33%. Data collection given on fertility and quality of life, ie global, digestive, urinary or sexual, will be presented.

**Conclusion:** In young women, conservative surgery for deep nodules using the shaving technique is feasible. Our study will assess, whether or not, favorable clinical outcomes may be obtained after a conservative surgical approach (i.e. favoring rectal shaving).

**Keywords:** rectovaginal endometriosis, QOL

## Poster - Quality of life

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### WOMEN'S EXPERIENCES OF ENDOMETRIOSIS: A SYSTEMATIC REVIEW OF THE QUALITATIVE EVIDENCE

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**Objectives:** An understanding of patients' experiences of illness improves clinician appreciation of the condition and enhances care. Little is known about women's experiences of endometriosis. The aims of this study were to synthesise evidence on women's experiences of endometriosis from research using qualitative research methods and to identify knowledge gaps.

**Design:** A systematic review of research using qualitative methods.

**Materials and Methods:** A systematic search strategy was employed to locate research that examined women's experiences of endometriosis using qualitative research methods. Papers meeting the inclusion criteria were subjected to quality assessment. Thematic analysis was used to synthesise the findings of the reviewed papers.

**Results:** Eleven studies reported in 18 papers met inclusion criteria and were included in the review. Participant numbers ranged from 15 to 61 women, typically recruited from support groups and specialised clinics. All studies were conducted in high-income, Anglophone countries. The main finding of this review was the wide-reaching impact of endometriosis on a woman's life. It was also clear that women are dissatisfied with the health care they receive. Many women experienced a significant diagnosis delay because of disbelief and normalisation of their symptoms by health professionals, friends, and family. There was a perceived mismatch between women's and health professionals' understanding of endometriosis-associated pain. Women often privileged the experiential knowledge of other women over medical information and clinician opinion.

**Conclusion:** Women's reported experiences of endometriosis demonstrated opportunities for improvement in current clinical practice and health policy. The needs of women with endometriosis extend beyond pain management. Assistance with the impact of the condition on all aspects of life is needed; this includes intimate and interpersonal relationships, employment, and emotional well-being.

**Keywords:** Endometriosis, qualitative, experience

## Poster - Quality of life

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### ASSESSMENT OF QUALITY OF LIFE AND DEPRESSION IN INFERTILE PATIENTS WITH OR WITHOUT ENDOMETRIOSIS: PRELIMINARY RESULTS

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**Objectives:** The aim of this study was to explore psychosocial effects of endometriosis on infertility patients using the Beck's Depression Inventory

**Design:** This is a prospective clinical study

**Materials and Methods:** One hundred and eight patients seen at an infertility clinic in Sao Paulo were invited to complete the Beck's Depression Inventory (BDI) and questions about their general health while waiting for their medical appointment. All respondents were informed about the objectives of the study and signed consent forms.

**Results:** BDI scores indicated that patients facing infertility were overall not depressed ( $9.0 \pm 0.8$ ; mean  $\pm$  SEM). The incidence of endometriosis in this group of women was 34.2% (36 patients). When BDI score was analyzed taking into account endometriosis, the group with the disease had a higher score than patients without it ( $10.6 \pm 1.6$  vs  $8.2 \pm 0.8$ ) although this difference was not significant and both groups were not depressed.

**Conclusion:** Women with endometriosis showed higher scores than women without it but the difference in their scores was not significant. Our data suggests that although suffering from a serious and many times debilitating disease, in addition to infertility, this group of women was not depressed.

**Keywords:** Endometriosis, infertility, depression

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### RIGHT PERI COLONIC ATYPICAL LESIONS AND GASTROINTESTINAL SYMPTOMS IN WOMEN WITH ENDOMETRIOSIS

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**Objectives:** demonstrate that adhesions on vermiform appendix, cecum and ascending colon caused by endometriosis atypical lesions can mimic vagal symptoms. Laparoscopic lysis of adhesions and appendicectomy can improve and cure this complains.

**Design:** 20 women with deep infiltrate endometriosis and chronic pelvic pain were enrolled in this prospective study. All complained of nausea, vomiting, heartburn and routine use of antacids drugs during menstruation

**Materials and Methods:** 20 women treated from deep endometriosis also had a thorough assessment of the pericolonc region since adhesions in this region can justify the digestive symptoms presented.

**Results:** 20 women treated from deep endometriosis also had a thorough assessment of the pericolonc region since adhesions in this region can justify the digestive symptoms presented. All of them presented with pericolonc atypical lesions. They underwent laparoscopic treatment for deep endometriosis disease and also lysis of right pericolonc adhesions plus appendicectomy. All women were carried out over 12 consecutive months after the surgery. The gastrointestinal symptoms improved completely.

**Conclusion:** Women presenting with pelvic endometriosis frequently report gastrointestinal complaints of increased intensity during menstruation. Right peri colonic atypical lesions can mimic vagal symptoms. Bear in mind that evaluation of the upper abdomen, are justified in women with gastrointestinal symptoms.

**Keywords:** Gastrointestinal symptoms endometriosis

## Poster - Surgical treatment

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### ROLE OF DEFUNCTIONNING PROTECTIVE STOMA IN COLORECTAL RESECTION FOR ENDOMETRIOSIS

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**Objectives:** The Objectives were to evaluate the rate of digestive complications –anastomotic leakage and rectovaginal fistula – after colorectal resection for deep infiltrative endometriosis (DIE) and to evaluate the role of protective defunctionning stoma (PDS) on the occurrence of these complications.

**Design:** We conducted a prospective cohort study including all patients undergoing a segmental colorectal resection for colorectal endometriosis with and without PDS in our center between 2003 and 2011.

**Materials and Methods:** All laparoscopically assisted and open colorectal resections were performed by two experienced surgeons, with an objective of complete resection of DIE. PDS was recommended for all patients requiring partial colectomy or multiple bowel resections. For patients requiring a colorectal resection and hysterectomy, omentoplasty was performed when feasible.

**Results:** During the study period, 198 patients had colorectal resection for DIE. Among them, 53 (27%) had a PDS. Overall, 15 (7.5%) digestive complications occurred: 9 (4.5%) rectovaginal fistulae and 6 (3%) anastomotic leakages. All rectovaginal fistulae occurred in patients with a low colorectal anastomosis ( $p < 0.0001$ ) and 88% (8 of 9) in patients with a partial colectomy ( $p < 0.0001$ ). No factors were associated with the occurrence of anastomotic leakage. The rate of rectovaginal fistula in patients with and without PDS was 9% (5/53) and 3% (4/146) ( $p = 0.06$ ). No anastomotic leakage occurred in patients with a PDS.

**Conclusion:** In this study, the risk of rectovaginal fistula is augmented in patients requiring both partial colectomy and low colorectal anastomosis for DIE resection. The protective effect of PDS remains unclear for these patients. Conversely, PDS seems not necessary for patients with mid colorectal anastomosis or low colorectal anastomosis without colectomy.

**Keywords:** Colorectal endometriosis

## Poster - Surgical treatment

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### A PRACTICAL PREOPERATIVE STAGING SYSTEM FOR ENDOMETRIOSIS USING TRANSVAGINAL ULTRASOUND - A RETROSPECTIVE ANALYSIS OF 200 CASES

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**Objectives:** To develop a practical and effective preoperative staging system for endometriosis using transvaginal ultrasound.

**Design:** A retrospective review of 200 patients who had pre-operative transvaginal ultrasound, office gel sonovaginography and laparoscopic surgery for endometriosis.

**Materials and Methods:** Specific ultrasound features were defined and a staging system developed to reflect the preoperative severity of disease. The stages were assigned numbers 1 – 4. The laparoscopic skill level required for surgery was then assigned based on the pelvic pathology encountered by the surgeon at laparoscopy.

**Results:** The preoperative staging system was compared with the laparoscopic skill level required for surgery to determine any correlation. The sensitivity and positive predictive value for predicting the need for surgical skill levels 6 and skill levels 1 - 2 was 88.5% and 79% and 93.9% and 92%, respectively. Overall, there was substantial agreement (Cohan's kappa 0.70) between our prediction of surgical skill level required and the actual skill needed for surgery using this staging system. The accuracy of predicting the exact surgical skills level required for surgery was 80.3%.

**Conclusion:** This new practical ultrasound based preoperative staging system correlates well with the level of surgical skill required to perform endometriosis surgery especially when there is minimal and severe disease. Large-scale multi center prospective studies will be needed to validate this staging system.

**Keywords:** Staging, laparoscopy, endometriosis

## Poster - Surgical treatment

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### THE LONG-TERM FOLLOW-UP OF LAPAROSCOPIC THERAPY FOR PELVIC DEEP INFILTRATING ENDOMETRIOSIS IN TEN YEARS IN PUMCH AND DISCUSSION ON THE CLINICAL TYPE

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**Objectives:** The aim of the study was to investigate the relationship between the anatomical distribution of DIE lesions and pain symptoms, the laparoscopic therapy, and the clinical type of DIE through a prospective study in ten years.

**Design:** This study was designed as prospectively between May 2003 and December 2012.

**Materials and Methods:** Clinical data from 1854 patients who were hospitalized in PUMCH suspected endometriosis and laparoscopically and pathologically diagnosed were collected, including 780 DIE patients and 1074 non-DIE patients. All of patients received the conservative laparoscopic surgery.

**Results:** The risk of pain symptoms in DIE patients were significantly increased. The longest operative duration (82.00±30.58min) and the postoperative hospitalization (7.67±2.08 days) were observed in rectum group. The median pain relief time was 56 months in the patients with complete excision of DIE lesions, which was significantly longer than that in patients with incomplete excision(25 months).Mutivariate analysis demonstrated that only incomplete excision of DIE lesions was a risk factor for shorter pain relief time.

**Conclusion:** DIE lesions were associated severe pain symptoms. The main distribution of DIE lesions was in the posterior pelvic compartment, and was more widespread and severe in DIE patients. Moreover, incision these DIE lesions are very important to treat the pain symptoms.

**Keywords:** Endometriosis, laparoscopy, tpye

## Poster - Surgical treatment

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### DOES OVARIAN SUSPENSION DURING LAPAROSCOPIC SURGERY FOR ENDOMETRIOSIS REDUCE POSTOPERATIVE ADHESIONS? A RANDOMISED CONTROLLED TRIAL.

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**Objectives:** Our study aim was to assess the effect of temporary ovarian suspension following laparoscopic surgery for severe pelvic endometriosis on the prevalence of postoperative ovarian adhesions. Ovarian suspension by suturing the ovaries to the anterior abdominal wall is a simple procedure used to facilitate ovarian retraction during endometriosis surgery.

**Design:** This was a prospective within group comparison double blind randomised controlled trial. We recruited women with severe pelvic endometriosis who required extensive laparoscopic surgery with preservation of the uterus and ovaries. Severity of the disease and eligibility for inclusion were determined at surgery.

**Materials and Methods:** After surgery, each woman was randomised to having only one ovary suspended. A new transabdominal suture was inserted to act as a placebo. Both sutures were removed 36 to 48 hours after surgery. Three months after surgery, a detailed transvaginal ultrasound scan to assess ovarian mobility.

**Results:** A total of 55 women were randomised to unilateral ovarian suspension for 36-48 hours, 52 of which were included in the final analysis. There was no significant difference in the prevalence of post-operative ovarian adhesions between the suspended and unsuspended side (38.5% vs. 51.9%) [OR 0.56 (95% CI. 0.22-1.35)](P=0.23). Post-operatively women reported significant improvement of all symptoms of endometriosis (P<0.01)

**Conclusion:** Temporary post-operative ovarian suspension for 36 to 48 hours following laparoscopic treatment of severe endometriosis does not result in a significant reduction in post-operative ovarian adhesions. Further work is required to identify more effective management strategies to prevent adhesion formation following extensive pelvic surgery.

**Keywords:** Ovarian suspension, adhesions

## Poster - Surgical treatment

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### MINIMALLY INVASIVE LAPAROSCOPIC MANAGEMENT OF URETERAL ENDOMETRIOSIS. ANALYSIS OF 70 CASES WITH A MEAN FOLLOW UP OF 36 MONTHS

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**Objectives:** To evaluate prospectively the efficacy of laparoscopic management of ureteral endometriosis.

**Design:** We have designed a prospective study.

**Materials and Methods:** We have followed 70 patients presenting with ureteral endometriosis from October 2008 to September 2013 submitted to laparoscopy to ureteral endometriosis resection.

**Results:** From 875 endometriosis cases operated from October 2008 to September 2013 in a private clinic, we have found an incidence of 8,0 % (70 cases) with preoperative evidence of moderate-severe ureter dilatation due to endometriosis. Dysmenorrhea (91%) and dyspareunia (64%) were the symptoms more frequently reported; but only 34 % (24 patients) had urinary symptoms and one patient had renal exclusion. In 68 cases, laparoscopic ureterolysis, in one laparotomic ureterocystoneostomy, and in 1 laparoscopic nephrectomy was performed. No major complications were found. The left ureter was affected in 80 % (n=56) of cases and disease was bilateral in just 3 cases. Median follow-up time was 36 months.

**Conclusion:** Laparoscopic diagnosis and management of ureteral endometriosis is safe and efficient. Preoperative planning should be rigorous, and complete surgical excision of ureteral endometriosis should be ensured by a team of experts familiar with endometriosis, and its management.

**Keywords:** Ureteral endometriosis, laparoscopy

## Poster - Surgical treatment

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### DEEP DYSpareunia AND RETRACTION POCKETS IN THE POSTERIOR CUL-DE-SAC

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**Objectives:** In patients with chronic pelvic pain suspicious for endometriosis, to evaluate any association of deep dyspareunia and/or retraction pockets (peritoneal windows) in the posterior cul-de-sac or uterosacral ligaments.

**Design:** Prospective, non-randomized, controlled study (Canadian Task Force classification, II-2). Women of reproductive age with chronic pelvic pain (for more than 6 months despite medical therapy, January 2012-June 2013), seen at the Saint Louis University Center for Endometriosis, and found to have endometriosis or not based on histology.

**Materials and Methods:** Consecutive patients with deep dyspareunia taken to surgery for suspicion of endometriosis were operated on by optimal laser excision. Retraction pockets and any lesions suspicious for endometriosis in the posterior cul-de-sac were completely excised and the presence or absence of endometriosis determined by histology.

**Results:** 134 patients with chronic pelvic pain and deep dyspareunia were taken to surgery. 109 (81.3%) were found to have endometriosis anywhere, with 101 (75.4%) having endometriosis in the posterior cul-de-sac or uterosacral ligaments (whether or not retraction pockets were found). 30 (22.4%) patients were found to have retraction pockets in the posterior cul-de-sac or uterosacral ligaments, of which 16 (53.3%) had endometriosis in the pockets. There was no statistically significant association found between endometriosis and retraction pockets in patients with deep dyspareunia. When retraction pockets were found, the majority had visible lesions consistent with endometriosis (24/30, 80%), but 1 in 5 (20%) did not. Of the 6 patients with retraction pockets without visible lesions in them, 50% (3/6) were found to have endometriosis at histology.

**Conclusion:** In patients with pelvic pain and deep dyspareunia, a high index of suspicion for endometriosis in the posterior cul-de-sac and uterosacral ligaments is needed. Retraction pockets – even without visible lesions - in these areas should be excised since half will have endometriosis on pathology. Larger multi-center trials are needed.

**Keywords:** Endometriosis, surgery, dyspareunia

## Poster - Surgical treatment

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### SURGICAL MANAGEMENT FOR COLORECTAL ENDOMETRIOSIS: IS A SYSTEMATIC DIVERTING STOMA RELEVANT?

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**Objectives:** To evaluate the benefit of systematic diverting stoma in patients undergoing surgery for colorectal endometriosis

**Design:** This was a retrospective multicenter study conducted in 5 centers

**Materials and Methods:** 47 patients had undergone rectal resection for rectal endometriosis by segmental resection or by disc excision. Two groups were compared: one with diverting stoma (group S) n= 33 and the other one without diverting stoma (group WS) n = 14. The complication rate and specifically the anastomotic leakage rate were evaluated

**Results:** the complication rate was higher in group WS than in group S : 57% versus 48% (p=0.75). The anastomotic leakage rate was higher in group WS than in group S: 3/14 (21%) in groupe WS versus 1/33 (3%) in group S (p=0.073). All patients from group WS required a reintervention for leakage's treatment whereas the patient from group S had only a medical treatment. In group S, all patients had a stoma closure 3 months after surgery. 2 of them required a stoma dilatation because of an anastomosis stenosis.

**Conclusion:** : in our study a diverting stoma seems to reduce the anastomotic leakage and its consequences. To reduce indication of diverting stoma, risk factors have to be defined in the population of young and healthy women suffering from endometriosis

**Keywords:** Rectal endometriosis, stoma

## Poster - Surgical treatment

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### THE ROLE OF TRANS VAGINAL ULTRASOUND (TVS) IN THE PREDICTION OF THE MOST APPROPRIATE ROUTE FOR SURGICAL MANAGEMENT OF WOMEN WITH ADNEXAL MASSES.

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**Objectives:** To evaluate the role of pre-operative transvaginal ultrasound (tvs) to predict most appropriate surgical route for the management of women with adnexal mass.

**Design:** Prospective observational study. A detailed preoperative TVS was performed by an experienced sonologist to assess the adnexal mass. Each lesion was classified using the IOTA protocol and the most likely histological diagnosis predicted using pattern recognition.

**Materials and Methods:** At TVS, the most appropriate surgical route was predicted (laparoscopy vs. laparotomy). If the adnexal mass was deemed to be benign, it is scheduled for laparoscopic intervention. Prediction of the laparoscopic route was deemed successful if the intention to treat was successfully completed laparoscopically.

**Results:** 108 women with adnexal masses were analysed. Based on the IOTA classification, 78.7% (85/108) of adnexal masses were classified as benign, 8.3% (9/108) borderline and 13% (14/108) malignant. The mean diameter was 84 mm. Pre-operative TVS successfully predicted the intention to treat laparoscopically with an accuracy of 97.2%, sensitivity 96.4%, specificity 100%, positive predictive value (PPV) 100% and negative predictive value (NPV) 88.5%. Pre-operative prediction of benignity, borderline and malignancy gave an accuracy 88% - 86.1% - 96.3%, sensitivity 93.9% - 28.6% - 91.7%, specificity 69.2% - 94.7% - 96.9, PPV 90.6% - 44.4% - 78.6% and NPV 78.3% - 89.8% - 98.9%, respectively.

**Conclusion:** In our unit, a detailed pre-operative TVS evaluation of an adnexal mass is useful in the triage of adnexal masses and the prediction of the laparoscopic surgery.

**Keywords:** Adnexal masses, ultrasound

## Poster - Surgical treatment

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### DEEP ENDOMETRIOSIS INFLICTING THE URINARY TRACT: LONG-TERM OUTCOMES OF SURGICAL MANAGEMENT

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**Objectives:** To investigate the intraoperative features and long term postoperative results of patients with urinary tract endometriosis.

**Design:** Retrospective review of medical records.

**Materials and Methods:** The records of all patients with urinary tract endometriosis were reviewed and the pre, intra and postoperative information of patients who underwent surgery was collected. Efficacy, safety and long-term outcome of laparoscopic treatment of bladder endometriosis and of those with ureteral endometriosis treated by ureteral reimplantation.

**Results:** During the study period, 69 patients with bladder endometriosis underwent surgery and seven patients with severe ureteral endometriosis underwent ureteral reimplantation. Laparoscopy was performed in all patients with bladder endometriosis and psoas hitch was the preferred technique for the ureteral reimplantation. Deep detrusor involvement was found in 45 (65.2%) patients. Of patients with bladder endometriosis, 21, 24 and 24 patients underwent partial cystectomy, deep nodule resection and nodule coagulation and ablation, respectively. No intraoperative complications were noted. After a median (range) follow up period of 60 (4-92) months, 92.7% of the patients were asymptomatic or reported improvement in symptoms. All but one patient with ureteral reimplantation reported significant symptomatic improvement. None of the patients needed additional medical or surgical treatment and no recurrence was noted.

**Conclusion:** After a long term follow-up we believe that laparoscopic excision a bladder nodule is a safe and efficacies approach. During surgery, full excision of bladder lesions should be performed. Ureteral reimplantation is a suitable technique in selected cases, gives good long-term results and no need for repeated surgical treatment.

**Keywords:** Bladder, ureter, laparoscopy

## Poster - Surgical treatment

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### EVALUATION OF THE EFFICACY OF DIFFERENT OPERATIVE TECHNIQUES IN THE TREATMENT OF PERITONEAL ENDOMETRIOSIS.

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**Objectives:** During surgical procedures we often encounter superficial peritoneal endometriotic plaques that may cause pelvic pain and adhesions. These lesions represent early stage endometriosis, which however may become the starting point of future scarred distortions and deep infiltrating endometriosis. Treatment solutions for superficial endometriosis are an issue of debate among physicians.

**Design:** Our aims to investigate the efficacy of various operative techniques for the treatment of superficial endometriosis in order to avoid local recurrence. During the treatment of these lesions we applied various instruments routinely used. We compared coagulation using a monopolar-, a bipolar electrode, vaporization using CO2laser to untreated full excision.

**Materials and Methods:** In 2011 we operated 52 patients using reproductive surgical technique whose procedures revealed superficial endometriosis. Inclusion criterion was the presence of 4 superficial lesions at different locations. All treated lesions by the above mentioned techniques were excised with intact border and the samples were analyzed if intact endometriosis remained.

**Results:** Tissue analysis of the samples treated by a monopolar electrode resulted in 42 positive (80,78%) and 10 negative (19,22%) cases, whereas for the samples treated by a bipolar electrode the results were 47 positive (90,38%) and 5 negative (9.62%) cases. Using the CO2 laser technique resulted in 15 positive (28,85%) and 37 negative (71,15%) cases. Tissue analysis of lesions using untreated excision resulted in 100% positive cases for endometriosis. Results of the investigation suggest that the techniques routinely used for the treatment of superficial endometriosis are of inadequate efficacy, as during the procedure upon coagulation of the lesions active endometriotic tissue is left behind promoting future recurrence and the appearance of more serious forms of the disease.

**Conclusion:** The key to avoiding recurrence is to eliminate all endometriotic tissue, not simply to treat them locally. Therefore we believe that the optimal solution for the treatment of superficial endometriosis is full excision using the shaving method.

**Keywords:** Superficial endometriosis

Poster - Surgical treatment

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**FOLLOW-UP AFTER URETERAL REIMPLANTATION ON 3 PATIENTS WITH DEEP INFILTRATING ENDOMETRIOSIS: TECHNIQUE AND FOLLOW UP**

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**Objectives:** To evaluate the intraoperative and postoperative results of 3 patients with ureteral endometriosis who underwent laparoscopic surgery for ureteral reimplantation.

**Design:** In this prospective study, we reviewed data of 3 patients with ureteral endometriosis treated by ureteral reimplantation.

**Materials and Methods:** We evaluated from July 2009 to July 2013, 350 patients submitted to a laparoscopic approach. The preoperative diagnosis was performed by a transvaginal ultrasound with bowel preparation and 3 patients (0,7%) were diagnosed with severe ureteral endometriosis, with hydronephrosis and underwent ureteral reimplantation.

**Results:** All cases had the left ureter compromised by the disease at pelvic portion of the ureter. Treatment consisted to adequate mobilization of the bladder, fixation of the posterolateral corner of the bladder to psoas (if necessary) and ureteral reimplantation with anti-reflux system all cases. We have performed a psoas hitch in two patients and a Leadbetter-Politano (direct uretero-neocystostomy) ureteric reimplantation technique in one patient. After a mean postoperative follow up period of 24 months, all patients reported significant symptomatic improvement regarding pain and renal function and two of them got pregnant spontaneously less than one year after the procedure. We have no recurrence during this follow up. No nephrectomy was done.

**Conclusion:** Bladder ureteral reimplantation is simple, effective and a first-line procedure for the replacement of the of the lower ureter. Should be performed by a multidisciplinary surgical team and is a suitable technique in cases of ureteral invasion of endometriosis with good long-term results regarding pain symptoms and infertility.

**Keywords:** Ureteral endometriosis, reimplantation

## Poster - Surgical treatment

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### FIRST SERIES OF 75 CASES OF LAPAROSCOPIC BOWEL RESECTION FOR COLORECTAL ENDOMETRIOSIS IN HUNGARY

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**Objectives:** With the present study we aimed to evaluate the outcome of the first consecutive series of radical laparoscopic resection of bowel endometriosis in Hungary.

**Design:** The surgical treatment of the colorectal endometriosis requires complete excision of all implants, but the modality of bowel resection is still debated. We describe the results of our experience in complete laser laparoscopic management of deeply infiltrating endometriosis (DIE) with colorectal involvement.

**Materials and Methods:** Between 10/07/2009 and 30/09/2013 at the 1st. Dept.of OB/GYN, Semmelweis University, Budapest a series of 75 multidisciplinary CO2-laser laparoscopic bowel resection was performed for colorectal DIE. The indication for surgery was a stenosis  $\geq 50\%$  and /or transluminal infiltration.

**Results:** During our procedures special care was taken to preserve the inferior hypogastric nerves and the inferior hypogastric plexus. A prospective database was established for all elective patients undergoing laparoscopic colorectal surgery by one surgical team. The main outcome measures assessed were operative duration, conversion rate, incidence of early complications, length of hospital stay, morbidity and mortality. Operative time (min, median, range) was: 186 (85-580). Non-colorectal DIE (number, %): 21(75), Laparoconversion (number, %): 4(5.3) Hospital stay (days, median, range): 6(3-10). Early major postoperative complications, Clavien-Dindo grade III or higher, (number, %) Total: 6(8). Natural orifice specimen extraction (NOSE) technique was used in 13.3% of cases.

**Conclusion:** Multidisciplinary nerve sparing laparoscopic colorectal resection for endometriosis is feasible and can be advised for selected patients who are informed of the potential risks of complications.

**Keywords:** DIE, laparoscopic surgery

## Poster - Surgical treatment

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### URODYNAMIC EVALUATION OF PATIENTS WITH DEEP INFILTRATING ENDOMETRIOSIS: A COMPARISON OF PRE- AND POSTOPERATIVE FINDINGS

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**Objectives:** To assess, by means of urodynamic testing, the pre- and postoperative urinary function of patients undergoing laparoscopic surgery for management of deep endometriosis

**Design:** A retrospective study that included eleven patients with deep endometriosis that underwent laparoscopy surgery.

**Materials and Methods:** 11 patients that agreed to pre- and postoperative urodynamic evaluation (convenience sampling, approximately 20% of all cases who underwent surgery for deep endometriosis in the study period). Urodynamic testing included uroflowmetry, cystometry, and pressure flow study. Testing was performed with a Dynapack MPX 816 P/Uromaster II 4.2 system .

**Results:** Median age was 37.1 (range, 24-53) years. Urodynamic findings were considered normal in 10 patients (91% of cases) preoperatively and in all cases postoperatively. Of the 11 laparoscopic surgeries performed, 45.5% of patients required ureterolysis and 63.7% underwent resection of the uterosacral ligaments.

Rectosigmoidectomy was performed in 45.5% of cases.

**Conclusion:** In our sample, the vast majority of patients with deep endometriosis had no demonstrable urinary abnormalities before surgery; preoperative urodynamic evaluation was within normal limits in 91% of patients. Comparison of pre- and postoperative urodynamic evaluation findings showed that laparoscopic endometriosis surgery had no effect on urodynamic parameters.

**Keywords:** Deep endometriosis, urodynamic

## Poster - Surgical treatment

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### **NODULECTOMY OR BOWEL RESECTION: IS THERE ANY DIFFERENCE IN THE CHARACTERISTIC OF THE RECTAL ENDOMETRIOTIC LESION?**

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**Objectives:** Compare and evaluate two techniques of laparoscopic treatment of deep bowel endometriosis: nodulectomy and segmental resection.

**Design:** Retrospective observational study, during the period from 2009 to 2013, of patients with bowel endometriosis who underwent laparoscopic treatment of the disease at the of the disease at the gynecological endoscopy and endometriosis clinic at Santa Casa Medical School, Sao Paulo – Brazil.

**Materials and Methods:** We evaluated 238 medical records of patients submitted to surgical treatment of rectosigmoid. Analysed variables were: technique of retossigmoidectomy (group A – linear nodulectomy and group B – segmental resection), age, injury characteristics (length, width, depth and volume) and postoperative complications. The statistical analysis used significant  $p < 0,05$ .

**Results:** 89 out of 238 records attended the inclusion criteria. Among the 89 selected patients, 46,1% were submitted to nodulectomy using the linear stapling technique and 53,9% the segmental resection technique. The results have revealed that the two groups showed the same profile age ( $p = 0.851$ ). The same did not occur when we analyze the extension, width, depth and volume of the lesions, in which linear technique showed lower extension ( $p < 0.001$ ), width ( $p < 0.001$ ), depth ( $p < 0.001$ ), and volume ( $p < 0.001$ ) when compared to the segmental technique. The complications found were 12 (13.48%) being 1 case (1.12%) of deep vein thrombosis, 1 of prolonged ileus, 1 of rectal bleeding, 1 stenosis of rectum, 2 cases (2.24%) of urinary retention, 3 cases (3.37%) of leakage and 3 rectal fistula.

**Conclusion:** The technique of linear nodulectomy was used for lesions of endometriosis whose length, width, depth and volume were smaller when compared with segmental technique. Both techniques are effective and safe, with overall complication rate of 13. 4%.

**Keywords:** Endometriosis, retossigmoidectomy, laparoscopy

## Poster - Surgical treatment

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### LAPAROSCOPIC PARTIAL CYSTECTOMY FOR THE TREATMENT OF BLADDER ENDOMETRIOSIS

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**Objectives:** To ascertain the value of laparoscopic partial cystectomy in the treatment of bladder endometriosis.

**Design:** This research was designed as retrospectively study

**Materials and Methods:** 24 cases of bladder endometriosis who were administered the surgery of laparoscopic partial cystectomy in Peking Union Medical College Hospital between Jan. 2006 and Aug. 2013 were analyzed.

**Results:** The most common symptoms in these patients were hematuria, frequency of urination during menstruation. The bladder lesions of 24 cases were excised completely by laparoscopy. The surgeries operated smoothly. There was complete relief of all the symptoms and no complications occurred. There was no recurrence in the following 24 months.

**Conclusion:** Laparoscopic partial cystectomy is the first choice of treatment for bladder endometriosis because of its minimal invasiveness, safety and effectiveness.

**Keywords:** endometriosis; bladder; laparoscopy

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### DEEP BOWEL ENDOMETRIOSIS: COMPARISON BETWEEN ROBOTIC AND LAPAROSCOPIC RECTOSIGMOIDECTOMY IN 380 PATIENTS IN A SINGLE CENTER

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**Objectives:** The aim of this study was to compare the outcomes of rectosigmoid resection using robotics or laparoscopy.

**Design:** We have designed a prospective study.

**Materials and Methods:** Between July 2009 and July 2013, 380 women were submitted to colorectal resection due to deep infiltrating bowel endometriosis. 360 patients were treated using just laparoscopy and 20 were treated using robotics. Groups were comparable regarding age, type, presentation of disease and indications.

**Results:** Blood loss was not measurable in all cases and mean hospital stay was 4 (3-5) days in both groups. There were no conversions to laparotomy in both groups. Rectosigmoidectomy was performed following the same surgical technique in both groups. There were no intestinal fistulas or anastomotic stenosis in both groups. Remission of intestinal symptoms was comparable in both groups.

**Conclusion:** Robotic rectosigmoidectomy for deep endometriosis is safe and effective. It presents advantages regarding precision, stable optics and better visualization. Future randomized studies comparing robotics and laparoscopy should be performed in order to better determine the role of the technique for the treatment of bowel endometriosis.

**Keywords:** Endometriosis, laparoscopy, robotics

## Poster - Surgical treatment

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### ROLE OF PROTECTION OSTOMIES IN ULTRALOW BOWEL RESECTIONS IN DEEP ENDOMETRIOSIS

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**Objectives:** To analyse the results of randomized trials regarding the ostomy protection and the best technique in ultralow rectal resection.

**Design:** A systematic review of randomized trials performed between 2002 and 2009 was performed to compare the use of a defunctioning stoma versus non stoma as well as the use of a ileostomy versus loop colostomy in patients with rectal ultralow resection.

**Materials and Methods:** Database includes articles published in the cochrane and medline. Four randomized studies were selected to the present systematic review, whose patients underwent rectal ultralow resection and it was compared the use of a defunctioning stoma versus non stoma as well as ileostomy versus loop colostomy to protect the anastomosis.

**Results:** 406 patients with average age of 60 years (all of them with lower rectal cancer) from four randomized clinical trials. It was not found randomized studies with the design involving patients with rectal endometriosis and evaluating the need for derivation. Three studies comparing stoma versus non stoma in lower rectal cancer revealed reduction of anastomotic leakage in patients receiving protective ileostomy in the qualitative analysis. In contrast to the most studies, one study that compared ileostomy versus colostomy recommended the last one, although well-designed randomized trials comparing both in ultralow anastomoses are scarce.

**Conclusion:** These recommendations are based on studies of rectal cancer patients, and we suggest its application in endometriosis, since the clinical differences of each disease are well-known and adequate to each situation.

**Keywords:** Defunctioning stoma

## Poster - Surgical treatment

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### HOW MANY SURGERIES ARE NECESSARY FOR DEFINITELY TREATMENT OF DEEP ENDOMETRIOSIS

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**Objectives:** Evaluate the number of surgeries required for definitive treatment of deep endometriosis in Reference Services in the State of Rio de Janeiro, Brazil.

**Design:** Retrospective study of 110 patients submitted to laparoscopic surgical treatment of deep endometriosis between September 2000 and July 2011

**Materials and Methods:** A questionnaire was answered in 110 consecutive patients. Analyzed: parity, initial clinical presentation, age at onset of symptoms and at diagnosis, number of previous surgeries performed to treat endometriosis, relief of symptoms after the first and last surgery and need for further surgical treatment. Descriptive statistical analysis: SPSS17.

**Results:** The mean age at diagnosis was 35 years and the average age of onset of symptoms was 27 years. 51% were nulliparous. Dysmenorrhea was the most frequent complaint (74.6%). Of the 110 patients evaluated, 43 (30.9%) had undergone previous surgery to treat endometriosis (minimum of one and maximum of seven surgeries). The average relief of symptoms after the first surgical treatment of 24 patients was 35.7% and after surgery in the Referral Center was 86.1 on a scale of 0 to 100.

**Conclusion:** Complete excision of endometriosis performed in Referral Center offers a good relief of symptoms. The excessive number of previous surgeries may be related to incomplete procedures, leading to a worse prognosis. Despite the complete surgery with expert staff, some patients have recurrence of symptoms, showing the inheritance of multifactorial disease

**Keywords:** Deep endometriosis, surgery

## Poster - Surgical treatment

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### ROBOTIC-ASSISTED LAPAROSCOPIC TREATMENT OF ENDOMETRIOSIS: EXPERIENCE FROM THE FIRST 71 CASES PERFORMED AT RIGSHOSPITALET IN COPENHAGEN.

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**Objectives:** Endometriosis may cause marked distortion of the anatomy. Laparoscopy can be challenging and require high skills. Robotic systems have been developed to facilitate laparoscopy. Only few reports addressing the use in endometriosis have been published. We present our results of robotic-assisted laparoscopic surgery for severe endometriosis.

**Design:** A consecutive case series of patients who underwent robot-assisted laparoscopy due to endometriosis.

**Materials and Methods:** Between May 2010 and June 2013, 71 patients underwent robot-assisted (Da Vinci Intuitive Surgical system) laparoscopy due to endometriosis. In Denmark treatment of severe endometriosis are centralized in two Centres and our Clinic is referral Centre for Eastern Denmark.

**Results:** The patients had endometriosis stadium II-IV (median stage IV). 37 patients had a history of one ore more surgical procedures for endometriosis. The surgical procedures included 18 hysterectomies, 58 cystectomies, 25 salpingo-oophorectomies, 3 bladder resections and 67 peritoneal excisions. 88% had significant adhesiolysis. The median time for surgery (including docking procedure) was 153 minutes. There were no conversions to laparotomy. The median blood loss was 30 ml (range 10-800). The right uterine artery was injured peroperatively in one case but no technical problems were observed. 91% of the patients were discharged from hospital within 24 hours. 7 patients had postoperative complications, 2 severe (one rectovaginal fistula and one leakage after bladder resection) and 6 minor (haematoma, cystitis).

**Conclusion:** Our results show that robot-assisted surgery for severe endometriosis is a feasible and safe procedure and can be performed without compromising the generally accepted principles for endometriosis surgery. However, data on the potential benefits of robotic-assisted laparoscopy in endometriosis are still lacking.

**Keywords:** Roboic-assisted laparoscopy, endometriosis

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**LINEAR STAPLER NODULECTOMY FOR THE TREATMENT OF DEEP INFILTRATING  
RECTOSIGMOID ENDOMETRIOSIS**

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**Objectives:** To evaluate the feasibility and safety of a more versatile nodulectomy technique using a linear stapler in cases of intestinal deeply infiltrating endometriosis

**Design:** A condition-specific bowel dysfunction quality of life questionnaire (Rome III – Constipation) was applied pre-operatively and post-operatively, in 59 consecutive patients who were operated on between January 2006 and February 2013.

**Materials and Methods:** 59 consecutive patients who were operated on between January 2006 and February 2013 were enrolled in this study, and 2 were excluded for not responding the questionnaire. Post-operative questionnaires were applied during the first week of April 2013.

**Results:** After a mean follow-up period of 19.2 months (3-84 months), no postoperative fistula or leakage was observed. In addition, no cases of rectal stenosis or bowel obstruction were recorded, and no patients were lost to follow-up. According to the Rome III questionnaire, no patients presented with worsening of bowel function, 12 patients (37.5%) remained unchanged, and 20 patients (62.5%) demonstrated improved bowel function

**Conclusion:** Linear stapler resection is a safe alternative to segmentar resection for endometriotic nodules on the anterior rectal wall and, apart from common belief, is not associated with an increased risk of bowel obstruction.

**Keywords:** Endometriosis, sigmoidectomy, nodulectomy

## Poster - Surgical treatment

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### CO-EXISTENT ENDOMETRIOSIS WITH FIBROIDS IN WOMEN UNDERGOING LAPAROSCOPIC MYOMECTOMY

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**Objectives:** To evaluate the prevalence of endometriosis and patient characteristics in women undergoing laparoscopic myomectomy for symptomatic uterine fibroids.

**Design:** This is a prospective study of all women undergoing laparoscopic myomectomy for symptomatic fibroids, with no previous diagnosis of endometriosis.

**Materials and Methods:** 212 women who underwent laparoscopic myomectomy during the study period, and all the cases were operated by a single surgeon to avoid operator bias. The demographic details, operative findings were prospectively entered into a database and analysed using SPSS software.

**Results:** Of the 212 women who underwent laparoscopic myomectomy, 45 had endometriosis (21%). Demographic details revealed 61% afro-Caribbean, 26% Caucasian and 13% Asian ethnicity. Fibroids are common in Afro-Caribbean women however by proportion endometriosis is less common in this group of women, being commonest in women of Caucasian and Asian origin. Women with endometriosis had less bleeding symptoms (20%) when compared with those without endometriosis (45%), but this was not statistically different ( $p=0.1$ ). Similarly there is no statistical difference between the two groups with regards to pain symptoms (31% with endometriosis, 23% without endometriosis experienced pain,  $p=0.07$ ). The size and number of fibroids didn't influence the prevalence of endometriosis in either group (In women with fibroids  $\geq 5$  cms, 80% had endometriosis and 86% of women didn't).

**Conclusion:** A quarter of the patients with symptomatic fibroids undergoing surgery were diagnosed with endometriosis. Patients with the concomitant diagnoses of both conditions were younger and presented with pelvic pain that was often disproportionate to the size of their fibroids.

**Keywords:** Laparoscopic myomectomy, endometriosis

## Poster - Surgical treatment

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### DEEP INFILTRATING ENDOMETRIOSIS TREATMENT WITH ROBOTIC ASSISTED LAPAROSCOPIC BOWEL RESECTION - PRELIMINARY EXPERIENCE WITH 22 CASES. A SAFE AND FEASIBLE ALTERNATIVE TO LAPAROSCOPIC APPROACH

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**Objectives:** The aim of this study is to present our preliminary results and evaluate the feasibility of robotic assisted laparoscopic colorectal resection for severe endometriosis.

**Design:** In this prospective study we evaluated women with endometriosis submitted to robotic assisted laparoscopic bowel resection.

**Materials and Methods:** Between September 2009 and September 2013, 22 women with colorectal endometriosis were submitted to surgery using the Da Vinci robotic surgical system. Parameters evaluated: short-term complications, clinical outcomes and long-term follow up, pain relief recurrence rate and fertility outcomes.

**Results:** Extensive ureterolysis was required in 18 women (82%). Fifteen women (68%) underwent ovarian cystectomy with removal of the cystic wall. Torus resection was performed in all women with unilateral or bilateral uterosacral ligament resection in two (9%) and seventeen (77%) women, respectively. In addition to segmental colorectal resection in all cases, partial vaginal resection was necessary in six women (27%). Four patients (18%) had also an appendectomy. Mean operative time with the robot was 157 minutes (range 90-190). Mean hospital stay was 3 days. Seven patients had complaint of infertility before surgery, with a mean infertility time of 2 years. After 12 months of follow-up period, all these women conceived (5 naturally and 2 of them were submitted to IVF).

**Conclusion:** We demonstrate that robotic assisted laparoscopic surgery for the treatment of deep infiltrating bowel endometriosis is feasible, effective and safe.

**Keywords:** Deep endometriosis, robotics

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### REPRODUCTIVE OUTCOMES AFTER LAPAROSCOPIC EXCISION OF DEEP ENDOMETRIOSIS AND FOCAL ADENOMYOSIS

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**Objectives:** To evaluate outcomes of laparoscopic excision of deep endometriosis and posterior focal adenomyosis.

**Design:** Retrospective study of infertile women with adenomyosis and deep endometriosis, who underwent laparoscopic surgery.

**Materials and Methods:** Thirty-nine women underwent laparoscopic excision of deep endometriosis and removal of posterior focal adenomyosis between April 2006 and December 2012. All 39 women (age: 34±3.6 y.o.) wished to conceive, and they had suffered from severe dysmenorrhea and chronic pelvic pain. The fertility outcomes of these patients were reviewed,

**Results:** There were no cases of serious complication during the operation. The operative time was (mean ± SD) 223±41 minutes, the volume of blood loss during surgery was 146 ± 96ml. Twenty women (51.3%, 20/39) subsequently conceived. Of these, eight women conceived spontaneously and 10 women conceived by IVF/ET, 1 woman conceived by intra-uterine insemination. Except 3 cases, 17 cases had conceived within 13 months after the surgery. Four women are still pregnant, one woman experienced spontaneous abortion. Fourteen women delivered by elective cesarean section. There were no cases of uterine rupture.

**Conclusion:** Laparoscopic excision of deep endometriosis and posterior focal adenomyosis is an effective surgery for women who wish to become pregnant. Since the period of time they can conceive is limited, they should be helped with artificial reproductive therapy.

**Keywords:** Deep endometriosis, adenomyomectomy

## Poster - Surgical treatment

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### RETROCERVICAL SEPTUM

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**Objectives:** To propose the term ‘retrocervical septum’ be added to the medical lexicon to designate the precise anatomical location of retrocervical endometriosis.

**Design:** Analysis of the century-long misuse of ‘rectovaginal septum’ to designate the anatomical location of retrocervical endometriosis.

**Materials and Methods:** Review of the literature on endometriosis from 1860 to 2013.

**Results:** Since the late 19th century retrocervical endometriosis has been designated endometriosis of the rectovaginal septum. The rectovaginal septum is a strong sheet of fibrous tissue that separates the lower vagina from the rectum. Endometriosis rarely invades the rectovaginal septum. A beautiful illustration of retrocervical endometriosis – endometriosis of the septum separating the posterior vaginal fornix from the rectovaginal pouch - was published in 1920, but mislabeled endometriosis of the rectovaginal septum. [Arch Surg. Sep 1920;1:215-283: Fig 42 (Case 16)]. Beginning in 1952 however, many authors correctly identified endometriosis of the septum between the posterior vaginal fornix and the rectovaginal pouch as retrocervical endometriosis. Endometriosis commonly invades the ‘retrocervical septum’.

**Conclusion:** The ‘retrocervical septum’ is a thin wall that separates the upper vagina and posterior vaginal fornix from the rectovaginal pouch. We argue that ‘retrocervical septum’ should be added to the medical lexicon and replace rectovaginal septum when describing retrocervical endometriosis.

**Keywords:** Retrocervical septum, Endometriosis

## Poster - Surgical treatment

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### URINARY TRACT ENDOMETRIOSIS - LAPAROSCOPIC SURGERY -

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**Objectives:** To describe our experience with laparoscopic surgery for the treatment of urinary tract endometriosis.

**Design:** Retrospective observational study of the management of patients with urinary tract endometriosis who underwent laparoscopic surgery.

**Materials and Methods:** Data from patients submitted to laparoscopic procedures due to deep infiltrative endometriosis performed at our Department, between June 2009 and October 2013, were reviewed. Cases with urinary tract involvement were selected.

**Results:** From 145 patients who underwent surgery, 41 (28%) had urinary tract endometriosis. Mean patient age was 34±5 years. 18 patients had moderate/severe dysuria; 2 had hematuria. 14 patients (34%) had bladder involvement (nodule size 11-44mm). Treatment consisted of nodule excision with partial cystectomy. 32 patients (78%) had ureteral involvement (48% bilateral, 26% left, 26% right). Bladder involvement coexisted in 5 cases and rectovaginal pouch endometriosis in 30 cases. Treatment consisted of laparoscopic ureterolysis (n=25) and ureteral resection with end-to-end anastomosis (n=2). Laparoscopic unilateral nephrectomy was performed in 5 cases of silent loss of renal function due to ureteral stenosis. Reported complications were: one traumatic dehiscence of bladder suture; one postoperative ureteral leak; two postoperative pyelonephritis. Mean follow-up was 12.4 months; 93% of patients are asymptomatic.

**Conclusion:** Our experience shows that bladder and/or ureteral involvement is not that rare in deep infiltrative endometriosis requiring surgical treatment and that laparoscopic approach is feasible and safe when performed by an experienced team.

**Keywords:** Bladder; Ureter; Endometriosis

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### FERTILITY AFTER LAPAROSCOPICALLY ASSISTED SEGMENTAL BOWEL RESECTION FOR RECTAL ENDOMETRIOSIS IN 22 CASES.

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**Objectives:** To evaluate the efficacy and safety of laparoscopically assisted segmental bowel resection for rectal endometriosis and resection of deep endometriosis for infertile women.

**Design:** Retrospective analysis of 22 (ages 29-42) infertile women with rectal endometriosis and deep endometriosis, who underwent laparoscopic operation.

**Materials and Methods:** Retrospective analysis of 22 infertile women with rectal endometriosis, who underwent laparoscopic radical conservative surgery. The operation was laparoscopically assisted segmental bowel resection for rectal endometriosis and resection of deep endometriosis at department of gynecology, Osaka Central Hospital.

**Results:** The average operative time was 332.6±47 min (mean±SD) and the average blood loss was 110.6±43.9ml (mean±SD). No conversion to open surgery was required, and all patients recovered without complications. All cases improved their symptoms. Three (13.7%) became pregnant naturally, one (4.5%) by means of AIH and five (22.7%) by means of IVF. Thirteen (59%) did not become pregnant in spite of their assisted reproductive therapy (ART). There are no pregnant cases, 2 years passed after the operation.

**Conclusion:** This study demonstrated that laparoscopically assisted segmental bowel resection is a safe and effective procedure for infertile women with rectal endometriosis and deep infiltrated endometriosis. But, sometimes it causes major complications, we need prudent decision for radical conservative surgery.

**Keywords:** rectal endometriosis, fertility

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**PREGNANCY RATES AFTER OPERATIVE TREATMENT OF ENDOMETRIOSIS IN TURKU  
UNIVERSITY HOSPITAL IN 2006-2010**

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**Objectives:** The aim of the study was to analyse the pregnancy rates after endometriosis surgery in Turku University Hospital from 2006 to 2010.

**Design:** Retrospective analysis from hospital records.

**Materials and Methods:** Turku University Hospital serves 250 000 people and almost all endometriosis surgery in the area is performed there. We studied the hospital records of operated endometriosis patients from 2006 – 2010 (N=390, mean age 34,7 years) with ICD codes (N80.1- N80.9) and the pregnancies from patients operated for infertility (N=75).

**Results:** During the study period the number of operations increased (N=65-85/year) as well as the percentage of advanced operations (15-29%). The use of laparoscopic approach increased (66-95%) especially laparoscopic advanced operations (10-86%). 19 % (N=75) of all operations were performed because of infertility. 37 (49%) of these patients conceived by spring 2012. Overall 49 pregnancies occurred (maximum 2 per patient). 36,7% of the pregnancies were conceived spontaneously and 63,3% following artificial reproductive techniques (ART). ART was needed only slightly more on patients with advanced operations (67%) when compared to those with minor operations (60%). Clearly less ART was required following laparoscopy compared to laparotomy (57% vs. 100%).

**Conclusion:** The use of laparoscopic approach and the number of advanced operations increased during the studied period. Subsequently a good number of pregnancies were reported by the patients operated for infertility.

**Keywords:** Endometriosis surgery, pregnancy

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### COMPLICATIONS ASSOCIATED WITH LAPAROSCOPIC SURGICAL TREATMENT FOR ENDOMETRIOSIS

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**Objectives:** To assess the incidence and type of complications in laparoscopic endometriosis-associated surgery in a tertiary-care university hospital.

**Design:** We performed a retrospective observational study

**Materials and Methods:** A series of 145 operative endometriosis-associated laparoscopies, performed between June 2009 and October 2013, were reviewed. Operative laparoscopy included minor procedures (minimal adhesiolysis, destruction of minimal endometriosis foci), major laparoscopic surgery (extensive adhesiolysis, ovarian cyst, moderate and severe endometriosis), and advanced laparoscopic surgery (hysterectomy and bowel resection).

**Results:** Deep infiltrating endometriosis affecting bowel and/or urinary tract was present in 72 patients. 48 hysterectomies and 6 bowel resections were performed. 138 patients had extensive adhesiolysis and 64 ovarian cystectomies were performed. Four major complications occurred: one intestinal injury complicated with adhesive peritonitis, one intestinal perforation and 2 urinary tract injuries. Six postoperative complications were noted. The overall complication rate was 9/145 (6,2%). The major complication rate was 4/145 (2,7%).

**Conclusion:** Laparoscopic surgical treatment for endometriosis seems to be safe with low major complication rate, especially when performed by an experienced surgical team.

**Keywords:** Endometriosis, laparoscopy, complications

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### MOISTENING PRETREATMENT OF SEPRAFILM IN LAPAROSCOPIC SURGERY IS A NOVEL, USEFUL, AND EASY TECHNIQUE FOR FUNCTION-SPARING SURGERY OF ENDOMETRIOMA

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**Objectives:** Seprafilm is rarely used in laparoscopic surgery because its insertion into the abdomen in laparoscopic surgery is difficult. We tested the usefulness of a novel technique of moistening Seprafilm before use to increase its flexibility before insertion through a trocar during laparoscopic surgery.

**Design:** A retrospective non-randomized open-label study

**Materials and Methods:** Laparoscopic surgeries that were followed by insertion of Seprafilm were evaluated in 67 women. A piece of Seprafilm (1/6 or 1/4 the size of a full sheet) was placed on gauze moistened with saline solution to soften it, then inserted through a trocar port, and placed at the intended site.

**Results:** A total of 245 pieces of Seprafilm sheets were pretreated and inserted via a 12-mm trocar port with a success rate of 100%, and placed correctly with a success rate of 80.0% (196 of 245 pieces). The mean total time required for placement of all pieces per surgery was 601 seconds  $\pm$  248.

**Conclusion:** Moistening pretreatment of Seprafilm is a simple technique that enables the film to be applied securely without breaking and without the need for special equipment in laparoscopic surgery. This new technique will most likely increase the frequency with which Seprafilm is used in laparoscopic operations for practical postoperative adhesion prevention.

**Keywords:** Laparoscopy, adhesion barrier

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### TOTAL PELVIC PERITONEAL EXCISION IN THE SURGICAL MANAGEMENT OF ENDOMETRIOSIS

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**Objectives:** This study aimed to establish the safety and effectiveness of total pelvic peritoneal excision in the treatment of endometriosis in terms of complications, re-operations, recurrences, adhesion formation, symptomatic relief and fertility.

**Design:** 169 patients with stage I-IV peritoneal endometriosis underwent laparoscopic total pelvic peritoneal excision. Patients were sent a postal questionnaire a mean of 3.4 years post-operatively and their notes were retrospectively reviewed a mean of 4.0 years post-operatively.

**Materials and Methods:** During total pelvic peritoneal excision, the majority of the pelvic peritoneum below the pelvic brim is excised including the peritoneum overlying the pouch of Douglas, ovarian fossae, bladder, ureters and pelvic sidewalls as well as the uterosacral ligaments. Amongst other procedures, temporary ovarian suspension was undertaken in 69.8% of cases.

**Results:** All cases were completed laparoscopically and the incidence of complications was low. 2-year and 5-year re-operation rates were 12.0% and 20.5% respectively. Proven peritoneal endometriosis recurrence as a proportion of total patients and patients undergoing re-operation was 4.7% and 26.7% respectively. All instances of peritoneal endometriosis recurrence were minimal and less severe than at initial operation, and in 62.5% of cases, recurrent lesions were located only outside the original excision margin. At long term follow up, at least a 50% reduction in the following symptom score was achieved in the following proportions of patients: pre-menstrual pain (63.9%); menstrual pain (68.5%); non-cyclical pelvic pain (81.6%); dyspareunia (76.8%); back pain (70.7%); dyschezia (84.3%); bladder problems (80.9%); heavy and/or prolonged periods (70.5%); pre-menstrual syndrome (75.0%).

**Conclusion:** Total pelvic peritoneal excision is safe and associated with a low re-operation rate, minimal and low rate endometriosis recurrence, long term symptom reduction and fertility. Long term ovarian preservation is possible in all patients with 'severe' and/or 'recurrent' endometriosis.

**Keywords:** Excision

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### INTESTINAL OBSTRUCTION FOR ENDOMETRIOSIS: A CASE REPORT

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**Objectives:** Report a case of intestinal obstruction caused by rectal endometriosis

**Design:** Intestinal Obstruction for Endometriosis: a case report

**Materials and Methods:** 30 years-old, female, nuliparous, was admitted to the emergency department with abdominal pain for 2 months, progressive, without changes in bowel habits. The patient was clinically subileus, without improvement. Physical examination with distended abdomen, decreased RHA. XR abdômen: signs of subileus. Blood tests: WBC 20,000 (5% rods), PCR 22.2.

**Results:** The patient underwent exploratory laparotomy on urgency performed right hemicolectomy and ileostomy for the treatment of intestinal obstruction. Investigation after surgery revealed deep endometriosis with intestinal involvement, submitted, eight months after laparotomy, laparoscopy for the treatment of endometriosis, with resection of rectosigmoid, oophoroplasty for endometriomas and endometriosis focus excision. During laparoscopic surgery, we opted not to perform reconstrucion of the intestinal tract so that the ileostomy would stay protecting the stapling line performed for the colorectal anastomosis.

**Conclusion:** The diagnosis of intestinal endometriosis requires attention to specific symptoms such as pelvic pain and dyschezia acyclic, besides the differential diagnosis with other intestinal affections. However, some patients may be asymptomatic, leading to delayed diagnosis and evolution to intestinal obstruction, like what happened with this patient.

**Keywords:** Endometriosis, obstruction, rectal

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### COMPLICATIONS AFTER SURGICAL TREATMENT OF ENDOMETRIOSIS

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**Objectives:** Evaluation of risk of complications post surgical treatment of endometriosis 5 (np2)

**Design:** Retrospective study of endometriosis patients treated surgically

**Materials and Methods:** Survey questionnaire and analysis of surgical skills

**Results:** Complications post surgical treatment of endometriosis appears as the rectovaginal fistula, the colorectal stenosis, the urethral fistula, the dyspareunia and the abdominal pain and/or dysmenorrhea in a decreasing classification. The most common after a surgical treatment of deep endometriosis is the colorectal stenosis which does not appear usually after laser treatment of endometriosis lesions

**Conclusion:** Colorectal stenosis is the more usual complication after surgical treatment of endometriosis

**Keywords:** Complications of endometriosis

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### SINGLE INCISION LAPAROSCOPIC SURGERY FOR A LARGE ENDOMETRIOTIC CYST

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**Objectives:** To describe a technique for the treatment of large benign ovarian cysts by single incision laparoscopic surgery (SILS) via the umbilical approach.

**Design:** Case report including discussion of surgical technique

**Materials and Methods:** X-cone single port system (Karl Storz) was employed in this surgery. Pre-bent atraumatic grasping forceps was used in conjunction with the straight laparoscopic instruments. We propose using a “to-fro” peeling technique in the z-axis in SILS cystectomy.

**Results:** The surgery was successfully completed without any complication encountered. The patient recovered rapidly post-operatively and was discharged well from the hospital. At the 1st month, slight bruising was noted peri-umbilical area. The bruise subsided rapidly within a week. At 6 months of follow-up, the umbilicus retained its depth and the patient appreciated the superior cosmetic outcome.

**Conclusion:** The proposed technique proved to be feasible, easy to employ and safe in SILS cystectomy, with the additional benefit of superior cosmetic outcome.

**Keywords:** laparoscopy, SILS, cystectomy