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The peritoneum is alive during surgery : from pathophysiology to the operative theater

ABSTRACTS

ABSTRACT SUBMISSIONS
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Topic : Surgical Meshes

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PREVENTION OF PROSTHTIC INFECTION IN VENTRAL HERNIA REPAIR. AN EXPERIMENTAL STUDY.

The aim of this study was to investigate how act different an antibiotic on a contaminated absorbable prosthesis (PGA-TMC) used for ventral hernia repair.

Eighty rats were included in this study. We have elaborated a defect on their abdominal wall (2 x 2 cms.) and covered by a prosthetic patch (PGA-TMC). Prosthesis were contaminated by *S. aureus* and impregnated with a Cephazolyne solution. Five weeks the animals were reoperated and later sacrificed.

Prosthetic infection decreased in all series of implants. Adhesions decreased at the same degree than infection. There is an optimun dosis of antibyotics, so an increasing in the dosis of Cephazolyne has not result in a higher reduction of inflammatory phenomenons.

Cephazolyne can prevent infection of PGA-TMC absorbable prosthesis. It can be very useful in cases of contaminated or emergency surgery for strangulated hernias or abdominal wounds having a loss of tissues.



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Topic : Intraperitoneal composite meshes (integration to the abdominal wall and adhesion prevention)

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Evaluation of adhesion formation, shrinkage and tissue response of four polypropylene-based meshes after intraperitoneal placement

This experimental study aimed to compare four types of polypropylene-based meshes in regard to adhesion formation, shrinkage and tissue response after intra-abdominal implantation.

In 32 male New Zealand rabbits, 4 different types of meshes of the same size (5.5cm × 4.0cm) were implanted intra-peritoneally in four groups: Group PP; polypropylene mesh implantation; group PP+e-PTFE; polypropylene-expanded polytetrafluorethylene composite mesh implantation; group TiPP; titanium-coated polypropylene mesh implantation and group PP-CSH; polypropylene-carboxymethylcellulose-sodium hyaluronate composite mesh implantation. At 90 days postoperatively, the animals were sacrificed and the extent of adhesions, the shrinkage rate and the degree of local inflammatory and fibroblastic reaction were recorded

In the PP+e-PTFE, TiPP and PP-CSH groups, the adhesions covered less than 25% of mesh surface, while in the PP group the adhesions covered more than 75% of the mesh surface ($p < 0.05$). Mean mesh shrinkage rate was more in the TiPP group (18.82%) in relation to the other three groups (PP: 15.64%, PP+e-PTFE: 13.98%, and PP-CSH:14.27%) and the difference was statistically significant ($p < 0.05$). The histological examination of mesh-tissue complexes revealed a predominance of fibroblastic reaction in the PP; PP+e-PTFE and PP-CSH groups, and a preponderance of inflammatory reaction in the TiPP group.

PP+e-PTFE and PP-CSH meshes should be considered for intraperitoneal implantation; as they combine minimal adhesion formation, minimal shrinkage rate, minimal foreign-body reaction and satisfactory connective tissue formation.



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Comparison of modified collagen matrix versus standard polypropylene in abdominal wall model for fascial reconstruction, two years rabbit study

We performed an follow-up study to investigate two implant materials currently used in different systems for treatment of incontinence and pelvic organ prolapse. Long-term host response and fate of the implant strength up to a two years period were compared in a rabbit model for fascial reconstruction. Monofilament Large Pore Polypropylene (Intepro LPP) is macroporous monofilament material while Intexen LP is novel modification of standard Intexen, not cross-linked porcine collagen acellular matrix.

Full-thickness abdominal wall defects were reconstructed, using “overlay” technique. Adult male New Zealand White Rabbits were used and randomly divided in two treatment groups of 18 rabbits each, according to the nature of the implant. Three implants of the same material per animal and fifty four implants in total per group were used. The fourth defect in each animal was repaired with continuous polypropylene suture, serving as internal control group. Three animals per group were sacrificed on day 30, 60, 90, 180, 365 and 730 days to evaluate morphologic and biomechanical properties of explants.

Two animals did not survive until the time of euthanasia: 1 from Intexen LP group with herniation and bowel incarceration and 1 from Intepro LPP group with unknown cause of death. In Intepro LPP group no reherniations, no seroma's, no infections were observed. Real herniations were found in total 7 out of 54 implanted Intexen LP constructs. Adhesions were comparable between groups. Tensile strength of the explants was significantly different at 90 and 365 days. Stronger foreign body reaction was observed against synthetic material, tempering over the time and initial strong inflammation around collagen matrix disappeared after 90 days.

One sixth of Intexen LP implanted meshes were herniated in in vivo abdominal rabbit model. Critical was a period of 90 days when most of the herniations occurred; at the same time point the material itself was a tearing point for more than two thirds of the explants (< 6 N/cm) and implants of Intexen LP were reaching barely 4 N/cm. Intepro LPP was integrated by an increasingly organised fibrotic scar within 60 days while Intexen LP was slowly replaced by thin collagen layer from 180 days on. After 2 years discrete leftovers of Intexen LP could be identified and at the same time no differences in tensile strength between materials were found.



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PERITONEAL ADHESIONS TO PROSTHETIC MATERIALS: AN EXPERIMENTAL COMPARATIVE STUDY OF TREATED AND UNTREATED POLYPROPYLENE MESHES PLACED IN THE ABDOMINAL CAVITY

Frequently hernia repair requires polypropylene (PP) meshes, carrying a well known adhesiogenic risk when placed in contact to intestine. The aim of this experimental study in a rat model was to assess the role of some materials, when combined with PP, in preventing the adhesions (AD) formation.

60 rats assigned to 5 groups for intraperitoneal mesh placement: untreated PP, PP+polyurethane (PU), PP+Surgisis (SIS), PP+ePTFE and control group without mesh. 21 days, 3 and 6 mo.s after the operation, assessment of AD formation, scoring AD in terms of extent and type and the Adhesion Index (AI).

No significant difference between PP+SIS, PP+PU and control in AD and AI. PP+SIS had significantly lower AD and AI vs PP+ePTFE. PP+PU had significantly lower AD and AI vs PP+ePTFE. Control group had significantly lower AD and AI than PP+ePTFE. PP had significantly more AD and higher AI vs PP+ePTFE.

Adhesions' incidence is reduced, using treated PP meshes. PP+PU and PP+SIS were superior to PP+ePTFE in adhesion prevention.



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Mesh shrinkage in sacrocolpopexy: fact or fiction?

This prospective study aims to evaluate the mesh shrinkage after a sacrocolpopexy in women with vaginal vault prolapse.

Women with symptomatic vaginal vault prolapse were recruited. All women self completed a Prolapse Quality of Life (P-QOL) questionnaire to assess the severity of prolapse symptoms and were examined using the POP-Q system by the same blinded clinician preoperatively and 6 months postoperatively. They all underwent sacrocolpopexy, performed by the same experienced surgeon using a standardised technique and a monofilament macroporous polypropilene mesh (Gynemesh). The mesh was visualised with a transvaginal ultrasound 5 MHz convex probe placed at posterior fourchette 3 days prior their hospital discharge and 6 months postoperatively.

Twelve women were studied. Eight women underwent a laparoscopic sacrocolpopexy whereas four women had an open surgery. The median and interquartile range of the distances between the perineum and the distal edge of the mesh measured three days and six months postoperatively were 1.3 cm (1.1-1.9) and 6.1cm (4.5 - 7.0) respectively (p value 0.002). The Wilcoxon Signed Ranks test was used (SPSS inc, Chicago, USA) to compare the ultrasonographic measurements.

Our data showed that shrinkage of these meshes do occur. Therefore, a new method as well as a correct technique of performing sacrocolpopexy needs to be developed to compensate for the shrinkage of the mesh. On the light of our data we might speculate stating that excessive tightening of the mesh should not be recommended since the fibrosis would further elevate the vagina leading to more successful outcomes and avoid the postoperative weakening of the posterior vaginal wall due to stretching. However a prospective randomised multicentre study and long term results are needed.



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Topic : Mesothelial repair

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Studies of TGF- β 1-3 in serosal fluid during abdominal surgery and their effect on in vitro human mesothelial cell proliferation

Increased transforming growth factor-beta (TGF- β) levels are associated with fibrosis, affected cell proliferation and post-surgical adhesion development, but the knowledge regarding TGF- β response to the surgical trauma is limited. This study investigated TGF- β 1-3 isoforms and fibrinolytic factors in peritoneal serosal fluid during abdominal surgery, together with the in vitro effect of TGF- β 1-3 on human mesothelial cell proliferation.

Total as well as biological active TGF- β 1-3 and fibrinolytic factors: t-PA, uPA and PAI-1 were measured in serosal fluid and plasma from 23 patients undergoing colorectal cancer surgery. In vitro proliferation of human primary mesothelial cell cultures upon TGF- β 1-3 stimulation was also investigated.

Total TGF- β 1 and TGF- β 2 levels were similar in serosal fluid and plasma while active fractions were increased in serosal fluid. In contrast, total fraction of TGF- β 3 was higher in serosal fluid compared with plasma, while levels of active fractions did not differ. Plasminogen activators (t-PA, uPA) were elevated while the inhibitor (PAI-1) was decreased, in serosal fluid compared to plasma. The in vitro mesothelial cell proliferation studies revealed that high TGF- β 1-3 concentrations decreased cell proliferation, while lower concentrations of TGF- β 1, similar to the levels found during surgery, increased mesothelial cell proliferation.

This human study shows increased active TGF- β levels in peritoneal serosal fluid, compared to plasma, during abdominal surgery and that TGF- β 1 at physiological concentrations, increased human mesothelial cell proliferation in vitro. TGF- β cytokines may be involved in post-surgical adhesion formation.



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Topic : Peritoneal Immunity and Surgery

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The Serine proteases uPA and PAI-1 act in concert with matrixmetalloproteinases and may conduct appendix perforation .

The Serine proteases are key factors in the proteolytic cascade and act together with the matrixmetalloproteinases (MMPs) in extracellular matrix (ECM) degradation. It is reasonable to assume that they may be involved in the genesis of tissue injury in appendicitis eventually leading to appendix perforation. The alteration of the balance between MMPs and their inhibitor tissueinhibitor of metalloproteinase (TIMP) during the course of the inflammatory process in acute appendicitis, was demonstrated in a recent study. In the present study special interest was focused on the expression and localization of serine urokinase type-plasminogen

The uPA and PAI-1 expressions were estimated in tissue specimens from patients with appendicitis (n=30), including phlegmonous, gangrenous and perforated appendicitis, and from control specimen (n=9) by means of the quantitative ELISA technique. The localization of the enzymes was performed by means of immunohistochemistry. The results in appendicitis were compared with controls and the results in the subgroups of appendicitis were mutually compared with each other and controls.

The over all expressions of UPA and PAI-1 were significantly higher in appendicitis than in controlspecimen ($p<0.001$) ($p<0.0001$). Expressions in phlegmonous (n=15), gangrenous (n=6) and perforated appendicitis (n=9) were each higher when compared with the controls ($p<0.01$) ($p<0.01$) (n=9). Moreover, when mutually compared PAI-1 was significantly higher in perforated appendicitis than in phlegmonous appendicitis ($p<0.01$).

uPA was observed in a patchy pattern in all groups of appendicitis and controls. PAI-1 occurred most intense in gangrenous and perforated appendicitis. The serosa stained intensely in specimen from perforated appendicitis.

The high expression of uPA and especially PAI-1 may be complementary to the MMPs in the genesis to a perforation in appendicitis. If uPA and PAI-1 are systemically reflected they could together with the MMPs predict perforation in patients with appendicitis, an advantage for future diagnose, treatment and outcome.



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SURGICAL TRAUMA INDUCES ELEVATED H₂O₂- AND LPO-LEVELS, DETECTABLE IN BLOODPLASMA AND PERITONEAL LAVAGE FLUID IN RATS

Polymorphonuclear cells play an important role in the healing process after damage of the peritoneum. Indirect evidence shows that ROS produced by PMN are a sequela of the inflammatory reaction caused by surgical trauma. Besides beneficial effects, the oxidative potential can result in additional tissue destruction. The amount of peritoneal damage is correlated to post-operative adhesion formation as well as to local tumor recurrence, and various studies have shown that administrating ROS scavengers leads to less adhesion-formation and tumor-recurrence. Surprisingly, the actual levels of the various ROS in vivo have never been reported.

According to our previously optimised adhesion-model, 7 animals (female Wag/Rij rats) were operated. In brief: a laparotomy was performed using a midline incision of 5 cm. A small oval was then excised on both lateral sides of the parietal peritoneum, simulating surgical trauma, after which the abdomen was closed in two layers. After 5, 24 and 48 hours, and in a second experiment after 5, 12 and 24 hours, peritoneal lavage was performed and blood samples were obtained. Samples of 3 non-operated animals were used as baseline values. After adding Butylated HydroxyToluene to all samples they were analysed spectrophotometrically.

Baseline-values of H₂O₂ in non-operated animals in lavage fluid and plasma were 1.265 ± 0.093 nmol/l and 1.875 ± 0.370 nmol/l respectively; baseline-values of LPO in lavage fluid and plasma were 2.799 ± 3.316 nmol/l and 1.362 ± 2.942 nmol/l, respectively. Five hours postoperatively the level of H₂O₂ rose to a maximum of 6.672 nmol/l and 7.391 nmol/l, in lavage fluid and plasma respectively. Animals which received scavengers showed decreased levels compared to baseline. The levels of LPO showed no change after 5 hours. The levels of LPO showed no change after 5 hours; After 24 hours all levels had returned to baseline value.

This experiment shows that it is possible to measure levels of ROS in plasma and lavage fluid. After surgical trauma these levels increase and this increase is avoidable by administration of ROS-scavengers.



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Topic : Endometriosis and the peritoneum

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The inflammatory-like microenvironment of a recent surgical procedure affects the attachment location, neoangiogenesis and growth of human endometrial tissue in a chimeric model of experimental endometriosis in mice.

Endometriosis is an opportunistic disease and many factors may independently promote a woman's individual risk for establishment of ectopic sites of endometrial growth. Using an experimental model of endometriosis, we have shown that matrix metalloproteinases (MMP) and vascular endothelial growth factor (VEGF) are required to establish ectopic human endometrial growth in the peritoneum of immunocompromised mice. Short-term exposure of human endometrial tissue to interleukin-1 β (IL-1 β) can also promote this disease in our model. Since IL-1 β can stimulate the MMP system and VEGF production in normal wound repair, acute peritoneal injury, such as oophorectomy, may affect the establishment of experimental endometriosis in our model.

Endometrial biopsies were obtained with written informed consent from normally cycling women during the late proliferative phase of the menstrual cycle. The use of human tissues was approved by Vanderbilt's Institutional Review Board. Biopsies were maintained in vitro as 1-2 mm organ cultures for 12-20 hrs prior to intraperitoneal injection into Rag2 Δ (c) mice at intervals (<24 hrs or 5 days) after oophorectomy and subsequent treatment of mice with an estradiol-releasing silastic capsule. Animals were euthanized at timepoints after injection of human tissue and the location and size of the ectopic lesions were noted. In some animals, vascularization of lesions was documented by immunohistochemistry using anti-CD105.

In mice receiving human tissue within 24 hours of oophorectomy, lesions were predominately located at the site of peritoneal injury. In contrast, mice receiving human tissue 5 days after surgery exhibited smaller lesions that did not preferentially localize to the injury site. Additionally, human tissue injection within 24 hrs of prior ovariectomy led to increased peritoneal vascularity and was associated with the development of multiple adhesions resulting in adherence of the uterus to the bowel and other peritoneal sites.

Surgical injury within the peritoneal cavity can significantly enhance the early invasion and vascularization of human tissues in an experimental chimeric model of endometriosis. This finding may have relevance to the development of endometriosis in women following a variety of recent surgical procedures. (This research was supported by the Eunice Kennedy Shriver NICHD/NIH through cooperative agreement U54 HD052668 as part of the Specialized Cooperative Centers Program in Reproduction and Infertility Research and NICHD/NIH R03 HD52012).



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Aberrant gene expression of cytokines in peritoneum and endometrium during the menstrual phase in women with endometriosis

Endometriosis is a chronic gynaecological disease commonly associated with pain and infertility, and significantly associated with retrograde menstruation . However, it is not well understood how normal peritoneum and eutopic endometrium may be involved in this pathogenesis. The aim of our study was to examine differential messenger RNA (mRNA) expression of relevant cytokines, aromatase, metalloproteases, growth and adhesion factors in normal peritoneum and in endometrium from women with endometriosis when compared with women without the disease during the menstrual and luteal phases of the cycle.

Peritoneal&endometrial tissues were selected from 35 patients during luteal (n=20)&menstrual(n=15)phase. Patients either had a laparoscopically normal pelvis(controls,n=11)orhad a confirmed endometriosis(n=24)as per ASRM stageI-II(n =12)&stageIII-IV(n=12).The mRNA levels of vimentin,vascular cell adhesion molecule(VCAM-1),integrins $\alpha 1 \beta 1$ & $\alpha 3 \beta 1$,interleukin(IL-1 β ,IL-6,IL-8),tumor necrosis factor(TNF- α),transforming growth factor(TGF- $\beta 2$),aromatase,metalloproteases (MMP)-3,regulated on activation normal Tcell expressed&secreted(RANTES),monocyte chemotactic protein(MCP-1)&intercellular adhesion molecule(ICAM-1)were evaluated using real-time RT-PCR.

Increased peritoneal mRNA levels of RANTES,VCAM-1,MMP-3,TGF- $\beta 2$,IL-6 & ICAM-1 and endometrial mRNA levels of MMP-3,TNF- α &IL-8 during menstrual phase were compared to luteal phase in women with endometriosis.During luteal phase endometrial IL-1 β & RANTES & peritoneal TNF- α & MMP-3 mRNA levels were increased in endometriosis compared with controls. During menstrual phase,increased endometrial expression of $\alpha 1 \beta 1$ & $\alpha 3 \beta 1$ integrin,combined $\alpha 1 \beta 1$ & $\alpha 3 \beta 1$ integrins, TNF- α ,IL-8,and MMP-3 mRNA levels & increased peritoneal expression of TGF- $\beta 2$,IL-1 β ,IL-6&ICAM-1 but decreased peritoneal MCP-1 mRNA levels in women with endometriosis when compared to controls

Increased cytokine mRNA expression in both normal pelvic peritoneum and in eutopic endometrium during menstruation may contribute to a pelvic inflammatory microenvironment favoring the development of endometriosis.

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An original in vitro model of endometrial cell adhesion to peritoneum: the early stage of pelvic endometriosis development

Endometriosis is defined as the presence of endometrial tissue outside the uterine cavity. Sampson's theory states that menstrual endometrial cells pass retrogradely through the fallopian tubes, attach and grow on peritoneal surfaces, leading to pelvic endometriotic lesion development.

In this study, we set up an original in vitro co-culture model, allowing quantification of human endometrial cell attachment to human peritoneal mesothelial cells obtained from the same patients. This original model may help us to better understand the adhesion process in endometriosis and to assess the effect of several molecules.

Endometrial and peritoneal samples were collected from patients undergoing laparoscopy for benign conditions. Endometrial and mesothelial cells were both enzymatically isolated using collagenase IA and cultured. At confluence, endometrial cells were collected and labeled with a fluorescent tracker (CFDA-SE). Labeled endometrial cells were then plated over confluent monolayers of mesothelial cells in 96-well plates at 5,000 to 40,000 cells per well. After 1 hour of co-culture, non-adherent endometrial cells were eliminated by washing, and fluorescence was measured to assess endometrial cell attachment to peritoneal mesothelial cells.

Culture purity was immunohistochemically evaluated using monoclonal antibodies to human CD10 and CK39, which are specific markers for endometrial and mesothelial cells respectively. The isolation procedure ensured cell purity of at least 90% for both cell types.

Endometrial cell labeling was also validated by fluorimetry, which showed a linear correlation with the number of labeled endometrial cells over a range of 500 to 50,000 cells ($r^2=0.99$).

Adhesion assays showed fluorescence readings that were linearly proportional to the number of endometrial cells placed on mesothelial cells per well over a range of 5,000 to 40,000 cells ($r^2=0.93$).

The pathogenesis of early endometriotic lesion formation can be divided into three crucial events: attachment of endometrial cells to peritoneal mesothelial cells, transmesothelial invasion, and proliferation in the submesothelial extracellular matrix.

We developed an original in vitro model of endometrial cell attachment to confluent mesothelial cells obtained from the same patients. This quantitative model facilitates study of the adhesion process in endometriosis and will allow us to compare attachment of endometrial cells from women with and without endometriosis, and to evaluate the role of hormones, cytokines, and growth factors.



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Metabolic consequences of oxygen added to the CO₂ pneumoperitoneum and types of ventilation during
laparoscopic surgery

CO₂-pneumoperitoneum causes acidemia, respiratory and metabolic acidosis. The addition of O₂ to the
CO₂ strongly reduces these effects. Here we wanted to define the consequences of O₂ addition to the
CO₂-pneumoperitoneum with different insufflation pressures in fixed and hyperventilated animal models.

CO₂ pneumoperitoneum created at intraperitoneal pressures (IPP) 10, 15 and 20 mmHg without and with
2% or 6% of oxygen, either low-fixed or high-hyperventilated 24 rabbits. Arterial blood gases (BG), acid
base balance (ABB), oxygen and lactate parameters were assayed every 15 min in 120 min.

All BG, ABB and metabolic parameters increased with elevated IPP. These changes were severe when
ventilation was fixed and disturbances were less pronounced when 2 or 6% of oxygen was added. The
IPP, amount of oxygen and ventilation were found to be independent variables affecting BG, ABB, O₂
values.

Absorption of CO₂ from the abdominal cavity increases with the IPP. The addition of small amounts of
oxygen to the CO₂-pneumoperitoneum reduces the metabolic consequences there off. It is suggested that
this is due to the prevention of metabolic and local tissue hypoxemia during CO₂-pneumoperitoneum.



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Changes of selected fibrinolytic system parameters in peritoneal environment caused by surgical manipulations

Tissue injury, bleeding and infection related to the intraabdominal surgical manipulations promote peritoneal adhesions. Decreased proteolytic activity of peritoneum seems to play a crucial role in adhesion formation.

In liver synthesized thrombin activatable fibrinolysis inhibitor (TAFI) is a key protein linking coagulation and fibrinolysis. Active TAFI(TAFIa) is a carboxypeptidase which retards plasmin formation, makes plasmin more susceptible to inhibition by antiplasmin and impairs fibrin polymerization. Thrombomodulin (TM), the cell surface receptor for thrombin, catalyses of TAFI activation and can be marker of endothelial injury. The role of TAFI and TM were not investigated in peritoneal adhesion.

TAFI and TM in peritoneal lavage (PL) fluid were examined both in patients undergoing long abdominal operations (Soave proctocolectomy, Nissen fundoplication and splenectomy – Gr.1), laparoscopic cholecystectomy (Gr.2) and uncomplicated appendectomies (Gr.3). Children with hernioraphy were controls. PL using 0,15 Mol NaCl (5ml/kg b.w., temp.37 gr. C), was performed after opening of peritoneum and before its closure. Samples were immediately centrifuged and frozen (-80oC). TAFI concentration(TAFIc) and activity(TAFIa) and TM concentration(TMc) were determined by ELISA with commercially available kits. TAFIc was presented as a percentage of TAFIc in standard plasma. TAFIa was determined by chromogenic assay.

Long operations caused statistically significant increase in TMc and TAFIc comparing to control patients. Laparoscopic cholecystectomy did not change both TM and TAFI concentrations in PL fluid. Interestingly, initial TAFIc and TAFIa values were ca 10 times lower comparing with both controls and open surgery cases, while TMc remained as high as in control group. Initial values of TAFIc and TMc in appeductomized patients were comparable with those in Gr.1 after operation. TAFIc and TMc in Gr.3 remained practically unchanged due to operation. TAFIa in Gr.3 was low both at the start and the end of operation comparable with hernioraphy patients.

Increased TAFIc and TMc in PL fluid after prolonged surgical procedures may play an important role in the progression of adhesion formation. This needs further investigation. Disturbances of peritoneal environment as an answer to infection in appendicitis probably trigger violent changes in coagulation-fibrinolysis system, even more expressed, then prolonged, elective intraabdominal procedures. Affection of homeostasis in laparoscopic access to peritoneal cavity comparing with open methods seems to be minimal, if measured using changes of hemostasis parameters.



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Clinical evaluation of peritoneal acidification and fibrinolytic response during laparoscopy, a randomized parallel group study comparing Helium and Carbon dioxide

For laparoscopy, pneumoperitoneum is mainly achieved using CO₂. This endogenous gas is safe, but alters acid-base balance both systemically and on the peritoneum. Local peritoneal fibrinolytic capacity is crucial in postoperative adhesion formation, but the impact of laparoscopic gases on these enzymes is unclear. The gas itself, or the flow of gas might change local biology.

Thirty patients, scheduled for laparoscopic cholecystectomy, were randomized to surgery, using CO₂ or He. Peritoneal pH was monitored throughout the procedure. Peritoneal tissue was sampled before and after creation of pneumoperitoneum, and during the procedure. Samples were analysed for t-PA, the t-PA activity and PAI-1 using ELISA technique.

Peritoneal pH directly dropped with CO₂ reaching 96% of initial values at 4 min, continuing to 91% during surgery. No changes were seen using He. Peritoneal t-PA decreased during surgery in both groups (CO₂: p=0.03, He: p=0.006), but higher levels remained after CO₂ laparoscopy (p=0.005). Peritoneal t-PA activity was maintained during surgery using CO₂, but decreased with He (p=0.004), a decline correlating with time (p=0.001).

CO₂ has an immediate acidifying effect on the peritoneum. Peritoneal t-PA decreased in both groups, but more t-PA remained at end of surgery with CO₂, along with preserved t-PA activity. The lowered peritoneal pH induced by CO₂ does not seem to negatively affect peritoneal fibrinolytic capacity.



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PERITONEAL DAMAGE IS CAUSED BY FLUID FLOW GENERATED BY PRESSURIZED IRRIGATION DEVICES

A prerequisite to adhesion formation is peritoneal damage. To assess the effect of pressurized irrigation on intact peritoneum an experiment was designed to analyse and measure five irrigation devices and their effect on intact peritoneum.

One, two and five (1, 2, and 5) second exposure of intact peritoneum by lactated Ringer's irrigation using currently available laparoscopic irrigation devices on porcine peritoneum. Fluid streams were directed at peritoneum for timed durations with biopsies of the areas evaluated by histology.

Fluid streams reached 2,500 cubic millimeters per minute. Tissue pressures ranged between 400 and 800 millimeters mercury (mm Hg) or 7.735-15.47 pounds per square inch. This resulted in dislodging and pressure washing peritoneal cells from intact peritoneum. Single cells, clumps of cells and sheets of peritoneum were found. The peritoneal defects and specimens were edematous and undermined showing evidence of unintended hydro- or aqua-dissection. A force of 550 mm Hg for 5 seconds uniformly resulted in peritoneal cell dislodgement. A pressure of 780 or greater for 1 second uniformly caused peritoneal cell loss from an intact surface.

Pressurized irrigation directed at intact peritoneum can damage, dislodge and strip away peritoneal cells causing defects and un-intended hydro-dissection.



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Attitudes and strategies for adhesion prevention in Sweden – A survey

Peritoneal adhesions is a long recognized clinical problem. Today it is generally accepted that minimally traumatic surgical technique leads to less adhesions. Adhesions cannot be avoided sufficiently using atraumatic methods alone. Additional adjuncts are needed. Today, several medical devices for adhesion control are available. They do not seem to have reached widespread use among general surgeons. To investigate the attitudes to adhesion prevention, and strategies adopted amongst surgeons to deal with adhesion formation, a survey was sent out to general surgeons practising in both university hospitals and county council hospitals.

An enquiry including 10 multiple-choice questions concerning attitudes to, and strategies for adhesion prevention was sent out to 300 experienced mainly colorectal and upper gastrointestinal tract surgeons in Sweden. 81,2% was specialists since more than 10 years. esMaker© was used to prepare the questionnaire and to analyse the results of the enquiry.

The response rate was 52%. 37% sometimes and 60% never use adhesion reducing agents. 15% consider their use when a second laparotomy is planned, 22% in operations where adhesiolysis is needed. 14% doesn't have any strategies and 39% never even consider their use. For 23% the reason is lack of knowledge about the products and for 40% lack of evidence in favour of their use. Half of the surgeons wants a 25-50% adhesion reduction to consider it worth while using an adhesion reducing agent. Another third would like a 50-75% reduction. Preferably, they would also like evidence that the product reduces bowel obstruction and female infertility.

Many surgeons never use adhesion reducing agents, because they find there is a lack of evidence of their efficacy, and because they simply don't have strategies for adhesion control. There are products available that meets the majority of the surgeons' demands when it comes to adhesion reducing effect, each with limitations. The question is if it is justified to completely avoid their use, in the light of the cost and clinical burden adhesion formation constitutes. There is a need for studies with clinical endpoints such as effect on SBO, but also education about the products available for adhesion reduction.



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The extra time needed to divide adhesions caused by previous surgery

The epidemiology, workload and cost of postoperative adhesion-related problems have been well documented. However, only limited amount of data has been published regarding difficulties encountered when re-entering the abdomen. The aim of this study was to evaluate accurately the time needed to divide postoperative adhesions and peroperative complications related to adhesions in a general surgical practice including both open and laparoscopic colorectal procedures.

A consecutive series of 111 patients scheduled for elective colorectal surgery and who had had prior abdominal or pelvic surgery were included in the study. Information regarding patient demographics, previous surgery, time taken to divide relevant adhesions during the operation and adhesiolysis-related complications were prospectively collected. In laparoscopic operations the extra time needed to fill the abdominal cavity with carbon dioxide and to insert the first trocar was measured as well. The adhesion division time was measured by stopwatch.

Patients had had altogether 189 previous abdominal or pelvic operations. 64 patients had had one, 23 two, 17 three, five patients had had 4 and two patients more than four previous operations. 12 of the previous operations had been performed laparoscopically. The mean and median time to divide adhesions were in open operations 20.9 min and 11.0 min, respectively. The corresponding times for laparoscopic operations were 9.1 and 3.6 min. The mean extra time needed for first trocar insertion was 1.0 min (range 0-8). There were two conversions due to adhesions, one inadvertent enterotomy and two serosal lesions requiring suturation.

The adhesions induced by previous surgery result in markedly increased surgery time, need for conversions to open surgery and peroperative complications. The incidence of serious peroperative complications is relatively low. The laparoscopic surgery in patients with previous abdominal operations is safe.



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Direct comparison of adhesion barriers in a rat model

A number of different adhesion barriers are now available in Europe and USA. However a direct comparison of their efficacy is difficult due to the differences in the pre-clinical models used in the literature. There are also no direct comparisons in humans either. Here we aim to directly compare Adept(R), Spraygel(R), Seprafilm(R) and Intercoat (R) in a single animal model.

In-vivo adhesion prophylaxis was assessed in a rat model involving traumatization by standardised electrocautery and suturing. Treatment with Adept(R), Spraygel(R), Seprafilm(R) or Intercoat(R) was compared to an untreated control group. Each group consisted of 15 animals and a total of 75 rats were operated. The relevant tissue was also examined histologically.

Adhesion formation was significantly reduced after treatment with the adhesion barriers than after no treatment. Coverage of the traumatized areas with adhesions was 79% in the control group. This was reduced to 54% by the liquid barrier Adept(R) ($p < 0.05$) and 59% ($p < 0.05$) by the gel barrier Intercoat and 46% by the solid barrier Seprafilm ($p < 0.01$).

There are significant differences in the efficacy of the currently available adhesion barriers.



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Adiponectin suppresses plasminogen activator inhibitor-1 induced by TNF- $\hat{\pm}$ in human peritoneal mesothelial cells

Plasminogen activator inhibitor-1 (PAI-1) in malignant ascitis was higher compared with non malignant ascitis. Previous reports suggest that PAI-1 may play an important role in angiogenesis and tumor growth. On the other hand, adiponectin, a circulating peptide hormone produced in adipose tissue, was reported to suppressed the development of tumor growth and peritoneal metastasis in nude mice. In this study, we evaluated the effect of adiponectin on the production of PAI-1 and tissue-type plasminogen activator (t-PA) in human peritoneal mesothelial cells.

Human peritoneal mesothelial cells (HPMC) were preincubated for 12 hours with various concentrations of human recombinant adiponectin (0.1, 0.5, 1.0, 10 and 20 $\hat{\mu}$ g/mL), then exposed to tumor necrosis factor alpha (TNF- $\hat{\pm}$)(10ng/mL) for 24hours. Levels of PAI-1 and t-PA mRNA in HPMC were assessed by the real-time reverse transcriptase polymerase chain reaction (RT-PCR) technique.

Incubation of HPMC with TNF- $\hat{\pm}$ resulted in significantly increased PAI-1 and decreased t-PA synthesis (Positive control). Adiponectin suppressed the expression of PAI-1 mRNA in HPMC in each dose. The relation between the expression of PAI-1 and the dose of adiponectin was not observed. On the other hand, t-PA mRNA in HPMC was not suppressed by adiponectin.

The results indicate that fibrinolytic capacity of peritoneal space is promoted because exposue of peritoneal mesothelial cells to adiponectin reduced the level of PAI-1 mRNA expression. This data suggest that peritoneal metastasis reduced by adiponectin may be mediated through reduction of efficient of angiogenesis and tumor growth by PAI-1.

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VIIIth PAX meeting

The peritoneum is alive during surgery : from pathophysiology to the operative theater

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Adding oxygen to the pneumoperitoneum and the influence on port site metastases

Port site metastases (PSM) are a frequent finding in advanced stage ovarian carcinoma. Different mechanisms are postulated to cause these PSM. In previous mouse experiments we observed a 50% reduction in tumorload after laparoscopy with addition of 4% oxygen.

In a RCT from 1-1-2007 we evaluated the incidence of PSM in 22 consecutive women undergoing a laparoscopy for suspected ovarian cancer with subsequent debulking laparotomy. Women were randomized to receive control laparoscopy with 100% carbon dioxide or 96% carbon dioxide with addition of 4% oxygen.

In the control group 19 port sites were excised, of which 9 (47%) showed PSM. In the oxygen group 16 port sites were excised and 8 (50%) showed evidence of PSM.

The occurrence of PSM is not only related to the use of CO₂ during exploratory laparoscopy. Other factors including direct wound contamination, aerosolization of tumor cells and episodes of desufflation and gas leaks known as the chimney effect are important and may be influencing this result.

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The peritoneum is alive during surgery : from pathophysiology to the operative theater

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Topic : Intraperitoneal intraoperative treatments : intraperitoneal chemotherapy and laparoscopic vaporization of treatments

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Non-Animal Stabilize Hyaluronic Acid (NASHA) is a useful vehicle to augment the effect of intraperitoneally administrated paclitaxel and cisplatin for peritoneal carcinomatosis.

Intraperitoneal (i.p) chemotherapy has been reported to be effective for peritoneal metastases. Here, we investigated the ability of Non-Animal Stabilized Hyaluronic Acid (NASHA) to retain the anticancer drugs in the peritoneal cavity and consequently to improve the efficacy of i.p chemotherapy.

In murine model to develop peritoneal metastases of gastric cancer cell line, MKN45, the antitumor effects of paclitaxel (PTX) or cisplatin (CDDP) were evaluated with the number of intra-peritoneal nodules or survival, without or with NASHA. Tissue concentration of PTX or CDDP in metastatic nodules was measured with HPLC.

In mice receiving PTX or CDDP with NASHA, the number of disseminated nodules were significantly reduced than in those without NASHA. The addition of NASHA significantly prolonged the survival of mice receiving CDDP treatment. The concentrations of PTX or CDDP in metastatic nodules were significantly increased by NASHA.

Our results indicate that NASHA increased the concentration of i.p administrated PTX or CDDP in disseminated tumor nodules and markedly enhanced antitumor effects of these drugs. NASHA is clinically useful as the vehicle for the i.p administration of anti-cancer drugs for peritoneal carcinomatosis.



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Molecular mechanisms underlying post-operative peritoneal dissemination might differ between a laparotomy and CO₂ pneumoperitoneum: a syngeneic mouse model with controlled respiratory support

The mechanisms promoting post-operative peritoneal dissemination are unclear. The objective of this study was to investigate post-operative tumor dissemination over time on both tissue and molecular levels.

C57BL6 mice were randomized into four groups of 32 animals each: anesthesia alone (control), CO₂ pneumoperitoneum at low (2mmHg) or high (8mmHg) intraperitoneal pressure (IPP) and laparotomy. A mouse ovarian cancer cell line (ID8) was injected intraperitoneally just before surgery. Groups were further sub-divided into three groups and a laparotomy was performed to evaluate dissemination on post-operative day (POD) 7, 14 or 42. Comparisons were made using the one-way ANOVA.

The incidence of invasion of cancer cells into the muscle layers of the abdominal wall was significantly higher in the laparotomy and high IPP groups than in the low IPP and control groups on POD 7 and 42. Expression levels of beta 1 integrin, cMet, uPA, uPAR and PAI-1 mRNA in the disseminated nodules were not significantly different among the four groups on POD7. However, expression levels of all of these genes in the disseminated nodules in the laparotomy group were significantly increased on POD14 compared to POD7. They then returned to controls levels on POD42. There were no significant differences in the expression levels of any of these genes among the groups at POD 42

The present study suggests that the molecular mechanisms underlying post-operative peritoneal dissemination might differ between a laparotomy and CO₂ pneumoperitoneum; therefore, strategies targeting post-operative tumor dissemination will likely need to account for the surgical environment.



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Impact of surgical peritoneal environment on postoperative dissemination and tumor growth in a preimplanted tumor model

We recently demonstrated that surgical peritoneal environment of CO₂ pneumoperitoneum at a low intraperitoneal pressure (IPP) could be optimal to minimize peritoneal dissemination, when tumor cells were inoculated just before surgery, in a syngenic mouse model. However, to mimic a clinical setting, a different study design in which tumors are present before surgery is also necessary. The objective of the present study was to evaluate the impact of surgical peritoneal environment on post-operative dissemination and tumor growth over time in a preimplanted tumor model. We used our established mouse surgical model with controlled respiratory support.

On day -7, C57BJ6 mice received an intraperitoneal inoculation of a mouse ovarian cancer cell line (ID8). On day 0, mice were randomized into four groups of 32 animals each: anesthesia alone, CO₂ pneumoperitoneum at low (2mmHg) or high (8mmHg) IPP and laparotomy. Groups were further subdivided into four groups and a laparotomy was performed to evaluate dissemination and tumor growth on post-operative day (POD) 1, 2, 7 or 14. Comparisons were made using the one-way ANOVA.

The peritoneal dissemination score was significantly higher in the laparotomy group compared to the remaining three groups on PODs 1, 2 and 7. We detected no significant difference in the peritoneal dissemination score among the low, high IPP and anesthesia groups on PODs 1, 2 and 7. However, there was no significant difference in the peritoneal dissemination score among the three surgical groups on POD 14. We detected no significant difference in the diaphragmatic dissemination score among the four groups on PODs 1, 2 and 7, whereas it was significantly higher in the three surgical groups than the anesthesia group on POD 14. Histopathological examination demonstrated that the incidence of invasion of cancer cells into muscle layers was significantly higher in the laparotomy group than the low IPP and anesthesia groups on POD 14. There was no significant difference in tumor growth among the four groups.

Our previous and the present findings suggested that a CO₂ pneumoperitoneum at a low IPP had few if any short term effects on peritoneal dissemination in either a tumor cells spillage or preimplanted tumor model.

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Novel Carboxymethylcellulose-Derived Hydrogel Prevents Postoperative Adhesions in a Rat Intraperitoneal Adhesion Model

Novel carboxymethylcellulose(CMC)-derived hydrogel in which phosphatidylethanolamine(PE) was introduced into the carboxyl groups of sodium CMC was newly developed. The purpose of the present study is to evaluate the efficacy of the CMC-PE in the prevention of postoperative adhesion in a rat model.

SD rats which received defects to their peritoneal wall and cecum were divided into four groups. In the preventive groups, CMC-PE, a mixture of CMC and PE or Seprafilm were applied. The control group received no treatment. Four weeks after, adhesions were scored and their strengths were measured.

The control group showed significant adhesions. CMC-PE-treated group showed a significant decrease of the adhesion score and strength. Moreover, they were lower than those of the Seprafilm-treated group. On the other hand, a mixture of CMC and PE-treated group showed significant adhesions.

The novel CMC-PE hydrogel was highly effective in reducing postoperative adhesions in this rat model, and the covalent binding of PE to CMC was important for this effect. This hydrogel may be appropriate for human clinical trials in open and laparoscopic surgical procedures.

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To close or not to close? Peritoneal non-closure and adhesion formation – results of a systematic review

Caesarean section (CS) is one of the commonest operations performed and the CS rate is on the rise. Previous studies showed that non closure of the peritoneum after surgery decreased operation time (RCOG 2002). Until recently, there has been little data on adhesion formation after closure versus non closure of the peritoneum after caesarean section. Several studies have since been published examining this clinical question.

We performed a systematic review on peritoneal closure versus non-closure in relation to adhesion formation in repeat caesarean section. The search strategy involved a thorough literature review using MEDLINE, Pubmed, EMBASE, and hand searching all the references cited in the relevant studies. All prospective studies that formally examined adhesions after repeat caesarean sections were included. To maintain clinical homogeneity, retrospective studies and studies that included the use of any anti-adhesion agents were excluded.

Eleven studies were identified according to our search strategy. Seven were excluded and four were included in our meta-analysis. Non closure of the peritoneum during CS resulted in increased adhesion formation (O.R. 2.49, 95% CI 1.47-4.19). In a subgroup analysis, more patients in the non-closure group had severe adhesions (O.R. 1.87, 95% CI 1.03-3.39).

This systematic review suggests that peritoneal non-closure results in more adhesions. It is an important finding as severe adhesions can result in delay in the delivery of the fetus with significant clinical consequences. The long term data from CAESAR study may throw some light on this issue in due course. In the mean time, it is important that clinicians understand the long term implications relating to adhesion formation and non-closure of the peritoneum after caesarean section.

Reference: RCOG, (United Kingdom) (2002) Peritoneal closure. Guideline 15



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Evaluation of a tranexamic acid supplemented fibrin sealant (Adhexil) in a rabbit uterine horn model of adhesions with and without bleeding, and in a model with two surgical loci

A rabbit uterine model was used to compare the efficacy of a tranexamic acid-supplemented fibrin sealant (Adhexil) & established devices. To separately identify any remote effect of Adhexil, a dual model (DUAL) added a cecal/sidewall injury.

In non-bleeding (NB) & bleeding (BL) model variants, animals (n=5/gp) were randomized to Control Adhexil, Seprafilm (SF), SprayGel (SG) or INTERCEED (INT - BL only) groups. In the DUAL model Adhexil was placed at both, neither or either loci. Adhesions were scored 13-16 d later.

Adhexil significantly reduced the adhesion extent (15 + 7%; 15 + 4%) versus Controls (74 + 13%; 78 + 9%) in the BL & NB models. SF (39 + 17%; 34 + 14%) or SG (61 + 18%; 43 + 14%, N=4) reduced adhesions non-significantly. In the BL model, INT (48 + 15%) only effected a modest reduction in extent.

In the DUAL model, Adhexil reduced selectively the extent & incidence of adhesions at the uterus & sidewall. The absolute and comparative performance of Adhexil in an established model of adhesions, together in the presence of bleeding justifies its further investigation as an adhesion barrier.



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Hyalobarrier® for Preventing Postoperative Adhesions: Systematic Review and Meta-analysis of Randomized Controlled Trials.

Among site-specific barriers used as adhesion prevention agents, there is evidence that a hyaluronan gel, Hyalobarrier®, made of ACP200®, an auto-crosslinked ester of hyaluronic acid without any foreign bridge molecules, may decrease the prevalence of postoperative adhesions in humans. This study is a meta-analysis of the available clinical evidence.

All clinical trials with Hyalobarrier® as adhesion reduction agent were searched and reviewed. Five randomized controlled trials (RCTs) met the inclusion criteria. Presence of adhesions at second-look was the outcome measure. Meta-analysis was performed using the surgery type as moderator. The effect measures were expressed as odds ratios (ORs) with 95% confidence intervals (CIs) and $p < 0.05$ was considered as statistically significant. Fixed effects model was used. Analysis was performed by using Comprehensive Meta Analysis software, version 2 (BIOSTAT, 14 North Dean Street, Englewood, NJ 07631).

Two RCTs were performed in laparoscopy ($n=79$) and 3 in hysteroscopy ($n=256$). When outcomes for overall 335 patients were examined, the presence of adhesions at second look was significantly lower in patients treated with Hyalobarrier® than in controls (OR=0.350; 95% CI=0.208-0.589; Z-value = -3.952, $p < 0.001$). Statistics of fixed effects analysis by surgery type demonstrated a significantly lower incidence of adhesions at second look in patients treated with Hyalobarrier® than in controls in both endoscopic surgery types: OR was 0.408 (95% CI = 0.217-0.766; $p=0.005$) in hysteroscopy and 0.248 (95% CI = 0.098-0.628; $p=0.003$) in laparoscopy.

This systematic review and meta-analysis showed that Hyalobarrier® could decrease the presence of postoperative adhesions after gynecological endoscopic surgery.



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Topic : Adhesion Prevention

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The extent of adhesion induction through electrocoagulation in an experimental rat study

Electrocoagulation is known to predispose to adhesion formation, yet electrocoagulation is used extensively to achieve haemostasis. The current study aims to investigate the role of electrocoagulation and suturing on peritoneal adhesion formation in a rat model.

Different modes of traumatisation were studied in 35 femal Wistar rats. The following groups were examined. Group 1: limited electrocoagulation (traumatisation with 40W for 1 second). Group 2: extensive electrocoagulation (traumatisation with 60W using greater pressure for 4 seconds). Group 3: mechanical denuding of the peritoneum. To study the the additive effect of suturing, experimental lesions were examined with additional suturing plus limited electrocoagulation (Group 4) or mechanical denuding (Group 5). Adhesion quantity and quality were scored 14 days post-operatively

Mechanical denuding of the peritoneum without damage to the underlying musculature lead to no adhesion fromation. After limited electrocautery, adhesion coverage of the traumatised area averaged 5%. This contrasted with extensive electro-cautery, where there was 65% adhesion coverage. If the lateral body wall was further traumatised by additional suturing then 71% and 62% of the traumatised areas were covered with adhesions for superficial electrocautery and mechanical denuding respectively.

Mechanical traumatisation limited to the peritoneum is a neglible factor in adhesion formation. However, additional traumatisation of the underlying musculature, either by deeper electrocautery or suturing, lead to significantly increased adhesion formation. These data show that there is a spectrum concerning the extent of traumatisation by electrocautery at the lower end of which there is little adhesion formation. Thus, clinicians should use smart coagulation systems and soft default settings to limit the depth of traumatisation whenever possible.



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adhesion prevention with A-part gel

Post-operative adhesion formation remains a major clinical problem with an incidence of 55-100%. Various studies have been performed in an attempt to find the perfect adhesion prevention method, but so far a maximum reduction of 20-50% has been obtained. The aim of this study was to test the promising effect of a new adhesion prevention gel (A-part, Braun Aesculap) and a new regenerating agent (RgtA).

A-part gel consists of polyvinyl-alcohol and carboxy-methylcellulose. A reproducible rat model was used to induce standardized adhesion formation in two following experiments. Experiment 1: 40 Wag/rij rats were divided in four groups of 10 animals. Control group; no agent used. Other three groups; A-part gel applied in the amount of 0,4ml, 0,8ml and 1,2ml respectively. Experiment 2: Control group; no agent used. Group 1 A-part gel 0,4ml, group 2 icodextrin 4% (Adept), group 3 RgtA. The percentage of adhesions to the defect was measured and the density was determined according to the Zühlke scale.

Experiment 1: 1,2ml as well as 0,4ml of the gel resulted in a significant reduction of adhesion formation (52,4%-60,1%). In addition, the density of the adhesions was significantly reduced with 45%. Experiment 2: compared to the control group both adhesion formation and the Zühlke score were diminished by the A-part gel (44,9% and 38,1% respectively). Icodextrin 4% and RgtA showed no significant reduction in adhesion formation.

The new adhesion prevention gel A-part appears to be a very effective adhesion prevention agent. A further improved application of A-part gel in adhesion prevention is presently investigated with the final goal to obtain a constant reduction of 50-100% adhesion formation.



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Preliminary results of a comparative randomized study in adhesion prevention : second-look evaluation shows significant results of Prevadh adhesion barrier

Post-surgical adhesions are a universal phenomenon whatever the surgical discipline is. In myomectomy, postoperative adhesions occur with an incidence of over 60%. The clinical consequences of these adhesions are multiple and potentially serious: they are implicated in 20 to 40% of secondary sterility problems in women and constitute the second cause of infertility. The aim of this comparative randomized study is to investigate the efficacy and long-term outcomes of a continuous and hydrophilic resorbable film (PREVADH-Sofradim-Covidien France) in preventing postoperative adhesion formation.

From May 2006 to February 2008, fifty-two patients aged 34 years \pm 5 years, undergoing myomectomy by open surgery, were randomly allocated to receive either PREVADH film or Ringer Lactate solution, directly applied to the uterine scars. Only patients with intramural and subserosal myomas larger than 6 cm were included in this study. The incidence, severity and extent of postoperative adhesions to the uterine scars were assessed during a laparoscopic second-look performed between 10-20 weeks. Postoperative follow-up is organized at 1 month, 1 month after second-look then each year during 3 years.

34 patients (18 patients in the PREVADH group, 16 patients in the control group) underwent laparoscopic second-look at 105.1 days \pm 47.5. Nine (50%) patients in PREVADH group and 15 (93.7%) in Ringer Lactate group demonstrate adhesions ($p=0.005$). Thus, 36 uterine scars were protected in PREVADH group and 27 in control group exhibiting respectively 33,3% and 81.5% of adhesions ($p=0.0001$). Mean severity scores was 1.2 \pm 0.4 in PREVADH group versus 1.6 \pm 0.5 in control group. Mean extent score was 1.6 \pm 0.8 versus 2.3 \pm 0.8 respectively. No serious adverse event related to PREVADH or control group was reported.

Myomectomy operations frequently result in pelvic adhesions which may impair fertility. PREVADH is effective in reducing adhesion incidence, severity and extent of uterine adhesion after myomectomy, demonstrating the need for adhesion prevention. PREVADH film acts first as a barrier and prevents adhesion formation. Its resorption restores the plan of a natural split between the structures previously separated by this barrier. The results of this multicentre randomized study show that PREVADH provides an efficient protection against gynaecologic postoperative adhesions and may have a favourable impact on long-term complications.

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Anatomical and functional results of transient ovariopexy after surgery for severe endometriosis

To assess efficacy (adhesions formation and subsequent fertility) and short and long term complications (ovarian endovaginal accessibility and ovarian antral follicle count) of transient ovariopexy after pelvic surgery for severe endometriosis.

Bicentric study including 188 severe endometriotic patients, 292 suspended ovaries, from 1997 to 2007. Adnexal adhesiolysis, deep pelvic endometriosis excision and endometrioma excision were done in 218, 96 and 132 cases. Surgical non systematic second look was done in 23 patients.

Easy, reproducible and painless technique. Immediate complication rate: 0.7%. Ovarian accessibility and reserve were not modified. Adnexal adhesion scores were decreased ($p < 0.01$). Global pregnancy rate was 52%. The best results were observed after using a monofilament thread.

Transient ovariopexy is a simple, reproducible and effective technique for adhesion prevention in severe endometriotic patients with very low morbidity and no effect on ovarian reserve. Subsequent fertility seemed improved. The thread used for this surgical tool had also an impact on results.



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Inpatient Care and Expenditures Associated with Abdominal Adhesiolysis in the United States in 2005

Post-operative adhesions frequently occur after abdominal surgery and are a leading cause of intestinal obstruction. Almost 90% of patients who undergo abdominal operations develop post-operative adhesions (Ray et al, 1998). Over time, the cost of adhesiolysis interventions has decreased. Increased use of minimally invasive surgical techniques, which may result in fewer inpatient days, has been identified as a potential contributor to this decrease (Ray et al, 1998). Using more recent data, and slight modifications to methods used by Ray et al (1998), we estimated inpatient care and expenditures attributed to adhesiolysis in the US.

Discharge data for patients with primary adhesiolysis (DRG 150 or 151) and secondary adhesiolysis (primary or non-primary ICD-9-CM procedure code for adhesiolysis, without DRG 150 or 151) were analyzed using the 2005 US HCUP Nationwide Inpatient Sample. Procedures were aggregated by body system via DRG codes. The number of adhesiolysis procedures, stratified by demographic and hospital characteristics, discharge status and primary payment source were calculated. Hospitalization rates per 100,000 persons were determined using US census data. Days of care and inpatient expenditures attributable to adhesiolysis, were calculated.

We identified 351,777 hospitalizations with adhesiolysis-related procedures (23.2% primary and 76.8% secondary adhesiolysis, respectively). The number of hospitalizations increased steadily by age, with the lowest rate for patients <25 years (5.2 per 100K), and highest for patients >65 years (88.4 per 100K). Women had a higher hospitalization rate than men (34.9 vs. 19.7 per 100K). Overall length of stay (LOS) was 7.8 days for primary procedures. There were 967,332 days of care attributed to all adhesiolysis related procedures, with inpatient expenditures totaling \$2.3B (primary \$1.4B and secondary adhesiolysis \$926M, respectively).

Compared to the Ray et al study, the US rate of adhesiolysis hospitalizations has remained constant over time (117.3 per 100K in 1994 [Ray et al, 1998] vs. 118.6 per 100K in 2005). However, overall LOS has decreased, as the LOS for primary adhesiolysis was 9.7 days in 1994 vs. 7.8 days in 2005. Total days of attributed care and volume of surgical procedures in the digestive system area have also decreased. Our estimates may be conservative, as they do not include indirect or other medical services' costs. Lysis of adhesions remains a costly problem in the US and should be of interest to providers and commercial and government payers.



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Prevention of postoperative adhesion formation in a laparoscopic mouse model

Pneumoperitoneum (PP) during laparoscopy has been shown to be a cofactor in adhesion formation. CO₂ pneumoperitoneum increases adhesion in time and pressure-dependent manner and this increase is reduced by adding 3-4% of oxygen to the pneumoperitoneum. Moreover, desiccation increases adhesions and hypothermia reduces adhesions. The aim of this study was to test the hypothesis that maximal adhesion prevention will be achieved by preventing sequentially the different adhesiogenic mechanisms.

Adhesions were induced during 60 min PP in a laparoscopic mouse model. Pure CO₂ (hypoxia model) or CO₂ with the addition of 3-4% O₂ (normoxia model) were used. The insufflation gas was humidified. Body temperature (BT) was strictly kept at 32°C or 37°C. First, the effect of adding 3-4 % O₂ to the PP in combination with lowering BT was analysed. Second, different products (antiinflammatories, ROS scavengers, calcium channel blocker, barriers, surfactant, flotation agents, antifibrinolytic products, etc) were tested in the hypoxia model. Third, some of these products were tried in the normoxia model and combined with low temperature.

The effect of adding 3-4 % O₂ to the PP and of decreasing body temperature was not additive. Adhesion formation was decreased by using SOD, ascorbic acid, dexamethasone, diltiem, wortmannin, Reteplase, phospholipids, Hyalobarrier gel and Spraygel in the hypoxia model (p<0.05 for all comparisons, Wilcoxon test). Maximal adhesion prevention was observed when dexamethasone, diltiem, Hyalobarrier Gel and phospholipids were combined with both adding 3-4% O₂ to the PP and reducing BT to 32°C (p<0.05 for all comparisons).

Firstly, the insufflation gas should be conditioned in order to minimize hypoxia and desiccation; this requires humidification of the gas and the addition of 3-4 % of oxygen to the CO₂. Moreover, cooling of the peritoneal cavity is important since it can decrease both the effects of hypoxia and of desiccation. Conditioning the insufflation gas, adhesion formation can be reduced by around 48% and this reduction can be increased to 58 to 90% by applying different prevention products.



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Topic : Peritoneal Imaging (preoperative and intraoperative and post-operative)

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Real-time monitoring of the adhesion formation/reformation process by sequential laparoscopy

Adhesions that form in the peritoneal cavity following surgery continue to be the primary cause of postoperative intestinal obstruction and may also produce infertility in women and chronic abdominal pain. Nowadays, there is much controversy over the adhesiogenic process and the long-term evolution of the adhesion tissue. The aim of this study was to follow the process of adhesion formation by sequential laparoscopy and to analyze the effectiveness of adhesiolysis in preventing adhesion reformation.

The experimental animals used were 16 male White New Zealand rabbits weighing 3000-3200 g. Animals were anesthetized and subjected to a longitudinal laparotomy performed along the midline. To the left of this incision, a 5 cm x 3 cm polypropylene mesh was placed on the parietal peritoneum and fixed using 6 transmural stitches of 4/0 polypropylene. Two study groups were established: Group I (control) (n=8) animals subjected to the mesh placement surgery; Group II (n=8) animals subjected to adhesiolysis 3 days after the mesh placement surgery. Adhesions to the implants were laparoscopically determined 3, 7, 14 and 90 days after surgery. At 90 days postimplant, the animals were sacrificed and samples harvested for morphological studies.

The percentage adhesion scores obtained for both groups 3 days postsurgery did not differ significantly. The adhesions were mostly loose, composed of a highly vascularized omental tissue. In control group, adhesions appeared as early as 3 days postimplant and were laparoscopically observed to stabilize during the first week. Beyond this time, no changes in these adhesions were detected on laparoscopy. In group II, no reformation was observed after adhesiolysis. Percentage adhesion scores revealed significant differences between the two study groups at 7, 14 and 90 days postimplant. At 90 days postsurgery, the resection areas were lined by a stable layer of mesothelial cells and showed a high degree of neoangiogenesis.

a) Adhesion formation was laparoscopically observed to stabilize between 3 and 7 days; b) Adhesion tissue resection and removal during the critical period of the adhesion formation contribute to reduce the mid- and long-term adhesion reformation.

PAX SOCIETY

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The peritoneum is alive during surgery : from pathophysiology to the operative theater

POSTERS

ABSTRACT SUBMISSIONS
PAX MEETING – CLERMONT-FERRAND
SEPTEMBER 18-20, 2008



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Topic : Tumor Cell Implantation

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Mucosal, tumour and peritoneal response to rectal radiotherapy

Rectal cancer treatment involves surgery and in selected cases radiotherapy. Pelvic radiotherapy is associated with increased morbidity such as impaired healing and adhesion formation. Further knowledge of cellular and molecular mechanisms are warranted.

Extracellular matrix (ECM) remodelling is elicited after radiotherapy and it is known that ECM remodelling is associated with adhesion formation. The aim of this study was to study enzymes involved in ECM remodelling and inflammation before and after preoperative radiotherapy.

Thirty-two patients with rectal cancer were included, of which, twenty patients received radiotherapy. Biopsies of rectal mucosa and tumour were taken before radiotherapy and during surgery 3-5 days after radiotherapy. They were later assayed with ELISA for MMP-1, MMP-2, MMP-9, uPA, PAI-1 and TGF-beta1. Biopsies of peritoneal tissues within and outside of the irradiated field were also taken during surgery and assayed for tPA and PAI-1.

MMP-2 levels were significantly higher in both mucosa ($p < 0.0001$) and in tumour ($p < 0.005$) after irradiation. MMP-1 and MMP-9 were not affected by radiotherapy. uPA ($p < 0.05$) in mucosa and PAI-1 in mucosa ($p < 0.01$) and tumour ($p < 0.005$) were higher in patients after radiotherapy.

The total and active fractions of TGF-beta1 were not affected, neither in mucosa nor in tumour.

No differences were seen in mucosa or tumour comparing between pre- and post-operative biopsies in patients not receiving radiotherapy.

Peritoneal biopsies did not display any difference in tPA and PAI-1 in relation to radiotherapy.

Radiotherapy elicits an activation of ECM remodelling enzymes mainly in mucosa, but also in tumour tissue. It is possible that follow-up may show that these enzymes can be used as indicators of radiotherapy induced injury and enable initiation of treatment to reduce the side-effects of radiotherapy. Remaining tumour cells could also use this activation to degrade the ECM and spread throughout the injured tissue. The lack of response to radiotherapy in peritoneum may be due to the timing of biopsies, as they were taken up to one week after radiotherapy. More investigations are warranted to investigate peritoneal response to radiotherapy.



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Prospective controlled randomized trial on Prevention of Postoperative Abdominal Adhesions by Icodextrin 4% solution after laparotomic operation for small bowel obstruction caused by adhesions (POPA study: Prevention of Postoperative Adhesions)

Adhesive small intestine occlusion (ASIO) is an important cause of hospital admission and are associated with significant morbidity and mortality, placing a substantial burden on healthcare systems worldwide. Icodextrin 4% solution (Adept, Shire Pharmaceuticals, UK) is a high-molecular-weight α -1,4 glucose polymer that is approved in Europe for use as an intra-operative lavage and a post-operative instillate to reduce the occurrence of post-surgery intra-abdominal adhesions. The current clinical study evaluates the safety and effectiveness of icodextrin 4% for decreasing the incidence, extent, and severity of adhesions in patients after abdominal surgery for ASIO

Methods The study project is a prospective, randomized controlled investigation. The safety and efficacy of icodextrin 4% is compared to no antiadhesion treatment (control) in a parallel group, prospective, randomized study with a blinded evaluation of efficacy end points. Subjects with ASIO and surgical indication to laparotomy are enrolled and randomized. Patients are submitted to adhesiolysis with bowel resection if necessary with or without anastomosis. The first group receives traditional treatment (control group) whereas the second group is treated with icodextrin 4% before abdomen closure.

Up to now 51 patients were randomized to have icodextrin 4% solution and 48 patients to have traditional treatment. The recurrence rate was 1.9% in the icodextrin groups vs 12.5% after a mean period of 18.2 months ($p < 0.05$). No complications icodextrin-related were found.

These preliminary data showed that the use of icodextrin 4% solution in ASIO is safe and can reduce the risk of re-obstruction.



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Topic : Intraperitoneal intraoperative treatments : intraperitoneal chemotherapy and laparoscopic vaporization of treatments

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COMPARISON OF CONTINUOUS AND FRACTIONATED ILLUMINATION DURING HEXAMINOLEVULINATE PHOTODYNAMIC THERAPY (HAL-PDT)

Fractionated illumination during photodynamic therapy (PDT) was shown to improve tumor response. This experimental study aimed to compare continuous and fractionated illumination in order to optimize hexaminolevulinate – PDT (HAL-PDT) in a rat tumor model with advanced ovarian cancer.

Intraperitoneal 106 NuTu 19 cells were injected in 36 female rats Fisher 344. Peritoneal carcinosis was obtained twenty-six days post tumor induction. Four hours post intra peritoneal HAL (Photocure ASA, Oslo, Norway) injection, two schemes of PDT were performed at 30 mW/cm² on a 1 cm² area: fractionated illumination (n=16) with a on-off cycle (“on”: 2 minutes and “off”: 1 minute) until a fluence of 30 J/cm² was delivered, and continuous illumination (n=20) with a fluence of 45 J/cm². Laser light was generated using a 532 nm KTP laser (Laser Quantum, Stockport, UK). Biopsies were taken 24 hours after treatment. Semi-quantitative histology was performed. Necrosis Value was determined: 0-no necrosis to 4-full necrosis.

HAL-PDT was efficient in producing necrosis irrespective of the scheme (NV=3.34 +/-0.91). Enhanced tumor destruction was superior with fractionated illumination compared to continuous illumination (3.67 +/- 0.70 vs 3.10 +/- 0.94) (p<0.05).

Fractionated illumination with short intervals should be considered for an effective HAL-PDT of advanced ovarian cancer.



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PROTOPORPHYRIN IX FLUORESCENCE PHOTOBLEACHING IS A USEFUL TOOL TO PREDICT THE RESPONSE OF RAT OVARIAN CANCER FOLLOWING HEXAMINOLEVULINATE PHOTODYNAMIC THERAPY

Accurate dosimetry was shown to be critical to achieve effective photodynamic therapy (PDT). This study aimed to assess the reliability of in vivo protoporphyrin IX (PpIX) fluorescence photobleaching as a predictive tool of the hexaminolevulinate photodynamic therapy (HAL-PDT) response in a rat model of advanced ovarian cancer.

Intraperitoneal (IP) 106 NuTu 19 cells were injected in 26 female rats Fisher. Peritoneal carcinosis was obtained twenty-six days post tumor induction. Four hours post IP HAL injection, a laparoscopic procedure (D-light system) and a fluorescence examination were made for 22 rats. The first group (LASER group, n=26) was illuminated with laser light using a 532 nm KTP laser on 1 cm² surface at 45 J/cm². The second group (NO LASER group, n=26) served as controls. Biopsies were taken 24 hours after PDT. Semi-quantitative histology was performed and Necrosis Value was determined: 0-no necrosis to 4-full necrosis. Fluorescence was monitored before and after illumination on complete responders (NV=3-4;n=20) and non responders (NV=0-2;n=6).

High PpIX photobleaching corresponded with complete responders whereas low photobleaching corresponded with non responders (p<0.05). A direct linear correlation was shown between photobleaching and necrosis (R²=0.89).

In vivo PpIX fluorescence photobleaching is useful to predict the tissue response to HAL-PDT.



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Educating patients about adhesions

We know that adhesions, what they are, the problems they cause, what should be done to prevent them and the available treatment options are rarely discussed with patients.

What are the reasons for this and what can be done to address this ?

Barriers to improving this situation are lack of time and knowledge/training of health professionals.

Questions and comments from patients and clinicians about adhesions sent via the website are being used to educate and provide information on the above. Based on information from current research a list of suggested questions that patients may wish to ask their surgeon has been compiled and is sent to patients on request along with more detailed information for patients undergoing surgery.

Comments received from patients and clinicians indicate that increased information is greatly appreciated and that they welcome being better informed by the provision of written information prior to surgery. They need time to be given the time and resources to do this. Patients also want to know what they can do themselves to minimize the risk of adhesion development and self-management and coping strategies.

Adhesions, their importance and relevance in surgery are generally not discussed with patients. Generating and encouraging interest amongst patients is key to driving research and ultimately improving standards. Patients should be signposted to sources of information on adhesions prior to surgery.



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Population pharmacokinetics and pharmacodynamics cisplatinum during intraperitoneal chemohyperthermia using a closed abdominal procedure

Peritoneal carcinomatosis is a metastatic diffusion of a cancer in the abdominal cavity and is associated with a bad prognostic. Since fifteen years, a therapeutic approach was developed: the hyperthermic intraperitoneal chemotherapy (HIPEC). Today, few pharmacokinetic data of the drugs used in this procedure are available.

The aim of this work was to study the pharmacokinetics of cisplatinum during “closed abdominal” HIPEC using population pharmacokinetic approach.

40 patients were treated between January 2003 and December 2004. Depending on their pathology, they received cisplatinum as single agent or in association with mitomycine C. Peritoneal and blood concentrations were used to develop a pharmacokinetic model for peritoneal and plasma compartments with NONMEM software. Different covariates were analysed in order to search those explaining a part of the interindividual variability of the pharmacokinetic parameters. Relationships between the areas under concentration-time curve (AUC) and haematological and renal toxicities as well as efficiency evaluated in terms of survival were explored.

Pharmacokinetics was modelised with a tricompartimental model. Estimations of plasma and peritoneal pharmacokinetic parameters were obtained. Few covariates especially weight, peritoneal carcinomatosis scores and association with MMC seem found significant. No direct relationship between peritoneal or plasma AUC and toxicity or efficiency could be demonstrated. The peritoneal/plasma AUC ratio is near 1 for cisplatinum, calling into question the peritoneo-plasma barrier concept. In order to determine the rate of cisplatinum transfert from peritoneum to blood, a single model integrating peritoneal data and blood data was developed.

Peritoneal and plasma pharmacokinetic during HIPEC could be modelised with multicompartimental models. Plasma model is pertinent and can be improved by introducing some covariates. This would make possible the determination of the optimal dose for each patient.



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Topic : Tumor Cell Implantation

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Morphine increases uPA production of mesothelial cells

We have previously reported that the provision of morphine in the drinking water to rats prevents experimental postoperative peritoneal adhesions (Khorram-Manesh et al., Dig Dis Sci 2006, 51:560-5). The aim of the current study was to investigate whether morphine affects some properties of a mesothelial cell line.

We cultured Met-5A, a human mesothelial cell line established from cells in the pleural fluid from non-cancerous individuals.

The expression of μ -opioid receptors (MOR) was investigated by immunocytochemistry, using a polyclonal rabbit antibody. Cell number was estimated by a cell proliferation assay kit (CyQuant). Production of urokinase type plasminogen activator (uPA) which is important for tumour cell invasion and metastasis, was measured by ELISA methodology.

MOR expression was demonstrated in the mesothelial cells, with cytoplasmic, as well as nuclear localization. Treatment of the cells with morphine (1 nM - 1 μ M) for 24 h, only marginally affected cell number, while morphine at 1 μ M increased uPA secretion markedly.

In the current study we demonstrated that the mesothelial cells express MOR. The nuclear expression is a puzzling finding. Moreover, morphine administration to the cells appears to cause increased uPA secretion which could be important for tumour cell implantation and spread. Therefore, we suggest that morphine treatment in cancer patients may contribute to disseminated disease.



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Topic : Surgical Meshes

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SHOULD ILCOCOCYGEUS FIXATION BE REINFORCED WITH ORGANIC MESH FOR TREATMENT OF VAGINAL VAULT PROLAPSE?

Ileococcygeal fixation (ILCF) has been firstly described in the 1963 as a vaginal surgical technique for treatment of vaginal vault prolapse. It has been proposed when the uterosacral ligaments were attenuated and not adequate for support. It has been reported an objective success rate of 53% and good patient satisfaction with this surgery on a visual analogue scale (VAS) (78/100) in a long term follow up of 21 months. The aim of our study was to evaluate whether the use of synthetic mesh to reinforce the ILCF might improve the objective as well as subjective outcomes.

Women with symptomatic vaginal vault prolapse â%¥ Stage II recruited from a tertiary referral gynecologic outpatient clinic were studied using POP-Q system, VAS and a prolapse quality of life questionnaire (P-QOL) to assess the severity of their symptoms and impact on QOL before, at 6, 12 and 24 months after surgery. All women underwent ILCF reinforced with organic mesh performed using a standardised technique by the same surgeon (group A). Women with similar demographic characteristics who underwent ILCF were used as case-control group (group B). Symptoms, QOL and POP-Q findings before and after surgery as well as between 2 groups were analysed.

78 women were recruited. The mean follow-up was 24 months (range 6–63). 41 women were included in group A and 37 in group B. 2 women of group A were lost at follow up. Pelvicol and Surgisis meshes were used in 19 and 20 women respectively. There was no significant difference between the 2 groups in the PQOL's domain scores and POP Q preoperatively ($p > 0.05$). There was no significant difference in the operative and recovery time, intra and postoperative complications between the 2 groups ($p > 0.05$). Although QOL and VAS significantly improved in both groups after surgery, they were not significantly different between the 2 groups postoperatively.

Our study showed that overall women in group A had significantly better outcomes than those of group B. Therefore reinforcing the ILCF using an acellular collagen matrix seems to improve the objective success rate. However further research with a large study population and long term follow up are needed to confirm our data.



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SIS graft for anterior vaginal wall prolapse repair: a case-controlled study.

The small intestine submucosa (SIS) is a biocompatible, acellular collagen matrix found between the mucosal and muscular layers of porcine small intestine which provides strength to the intestinal wall and consists predominantly of collagen. It acts as a natural extracellular matrix scaffold for host cell incorporation and tissue remodelling. It is infiltrated and replaced by host tissue within 90–120 days after implantation. At present there is limited data on its use for repair of anterior vaginal wall prolapse (AR). The aim of our study was to compare the prolapse quality of life (QOL) and examination findings between AR and AR with SIS.

Women who underwent traditional AR with and without SIS graft (SG). All women were assessed preoperatively and at 6 and 24 months postoperatively using a validated prolapse quality of life questionnaire and pelvic organ quantification system (POP-Q). QOL outcomes included the following: General health perception, Prolapse impact, Role limitations, Physical limitations, Social limitations, Personal relationships, Emotions, Sleep/Energy, and Severity measures. The POP-Q measured nine specific points relating to the anterior and posterior wall of the vagina, vaginal apex, genital hiatus (GH) and perineal body (PB).

14 consecutive women underwent traditional AR and 14 underwent AR reinforced with SG. At 6-month follow-up, the SG repair group showed significant improvement in all QOL parameters measured. In comparison to traditional AR, it was significantly better in improving role limitations, physical limitations and emotions. Both operations significantly improved prolapse QOL severity measures. SG repair improved all POP-Q measurements significantly, except total vaginal length (TVL), whereas traditional AR improved some measurements AA, BA, C, AP, BP, but not D, TVL, GH and PB. At 2-year follow-up there was no significant difference between 2 groups.

Surgery for vaginal prolapse results in marked improvement in QOL and prolapse severity. The greater improvement seen initially in the SG anterior group was not seen at 2-year follow-up. The lack of benefit of SG repair over traditional AR at 24 months highlights the fact that the evaluation of any new procedure requires at least this length of follow-up. This also questions the utilisation and cost-benefit of SG use for anterior vaginal wall prolapse. A larger longer-term study with patients randomised to SG or traditional AR with both subjective and objective evaluation is required to fully evaluate the use of SG for the AR.

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Topic : Endometriosis and the peritoneum

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Quantity and quality of retrograde menstruation: red blood cells, inflammation and peritoneal cells

The purpose of this study was to test the hypothesis that retrograde menstruation is associated with a higher concentration of endometrial cells in peritoneal fluid (PF) and with increased white and red blood cell concentration in PF when compared to nonmenstrual phases of the cycle.

PF was obtained at laparoscopy from 107 women with endometriosis and healthy controls, classified as per ASRM stage: I(n=25), II(n=20), III(n=6) and IV(n=8). Samples were collected during luteal(n=46), follicular (n=33) or menstrual(n=23) phase. Cell counts (leucocytes, erythrocytes, thrombocytes) were determined on cell counter. From a subset of 32 women (n=13 with a normal pelvis; n=19 with endometriosis) the PF was fixed, processed & thinlayers were prepared. Immunocytochemical stains were performed using monoclonal antibodies cytokeratin 7(CK 7), CK 8/18, Ber-Ep4 (epithelial marker), vimentin (stromal marker), calretinin&CD68 (macrophage marker).

Analysis of PF during menstruation (n=23) showed increased concentration of leucocytes ($3.3 \times 10^9/L$ vs $0.8 \times 10^9/L$, $P=0.03$), eosinophilic ($0.1 \times 10^9/L$ vs $0.04 \times 10^9/L$, $P=0.09$) and basophilic ($0.2 \times 10^9/L$ vs $0.04 \times 10^9/L$, $P=0.002$) granulocytes, erythrocytes ($0.3 \times 10^{12}/L$ vs $0.02 \times 10^{12}/L$, $P=0.006$), hemoglobin (0.8 g/dL vs 0.1 g/dL, $P=0.01$) when to nonmenstrual phases of the cycle. In 59 women with endometriosis, the PF concentration of erythrocytes was high during menses (n=15, $0.3 \times 10^{12}/L$) & decreased significantly ($P=0.001$) during follicular (n=21, $0.1 \times 10^{12}/L$) & luteal (n=19, $0.02 \times 10^{12}/L$) phase. In 2 patients during menses positive cells for Ber-Ep4 were observed.

Retrograde menstruation is associated with higher peritoneal inflammation, increased hemoglobin concentration in PF when compared to nonmenstrual phases of the cycle, but the presence of PF endometrial cells requires more investigation.



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Topic : Surgical Meshes

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**HISTOLOGICAL GROUND OF MESH APPLICATION IN SURGICAL TREATMENT OF GENITAL
PROLAPSE.**

We study collagen structure of connecting tissue among female patients with genital prolapse.

We study 121 patients with POP and systemic inconsistency of connecting tissue. We capture parts of pelvic floor structures and make a immunohistochemical study.

We found a significant decrease of collagens type 1, 3 in patients with not significant ICT. Patients with medium ICT has substitution of collagens type 1,3 on collagen type 4. In significant ICT were no collagens type 1,3 and 4.

Surgical treatment of genital prolapse in patients with inconsistency of connecting tissue required mesh fixation of vaginal vaults, because were is no collagen structure of own tissues and they have a high risk of genital prolapse recurrence.



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Indications of laparoscopic re-operation after sacrocolpopexy

Several studies have shown that sacrocolpopexy is associated with a low complication rate (5-10%) including vaginal exposure, de novo urinary stress incontinence or prolapse recurrence. Most of these complications can be treated vaginally. However, in some cases, abdominal surgery may be unavoidable. The aim of this study was to assess the indications of re-operation by laparoscopy following a sacrocolpopexy performed either by laparotomy or laparoscopy.

We conducted a retrospective monocentric study, at the centre hospitalier universitaire de Strasbourg, France. We identified seven patients with laparoscopic surgery for any complication after an abdominal sacrocolpopexy, from January 1st, 2004 to March 31st, 2008. Previous pelvic surgery, sacrocolpopexy procedure (number of meshes), clinical symptoms, time between sacrocolpopexy and re-operation, indication of re-operation and per-operative procedure were studied.

Quite all patients (6/7) had undergone previous pelvic surgery. Indications of the re-operation were: mesh exposure (4/7) with vaginal fistula through anterior or posterior meshes (3/7), prolapse recurrence (2/7), and chronic cystalgia (1/7). Mean time between sacrocolpopexy and re-operation was 22 months (3 to 58 months). Removal of one part or of the totality of the mesh was necessary in 6 cases. Despite this new procedure, three patients have shown post-operative complications.

Sacrocolpopexy for treatment of prolapse in the young women appears to be an efficient technique with low rate of complications, but, when it occurs, a total removal of the mesh by laparoscopic surgery seems to be necessary. All the patients of the study underwent a sacrocolpopexy with 2 meshes. In 3 cases we reported a fistula at the union of 2 meshes. Future studies should evaluate to perform sacrocolpopexy with one mesh fixed to the promontory.



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Transvaginal hydrolaparoscopy and electrocautery of the ovarian capsule in PCO patients

Aim: to evaluate the feasibility of drilling of the ovarian capsule using a transvaginal endoscopic access.

PCOS anovulatory women, clomiphene resistant or with failure of ovulation induction with gonadotrophines, were referred for electrocautery of the ovarian capsule using a transvaginal endoscopic access. For the purpose of drilling of the ovarian capsule, we use a 5 Fr bip

39 patients mean duration of infertility 26.5 m (SD \pm 2.6), mean age 30.4 y (SD \pm 3.8), mean BMI 29.4 (SD \pm 9.7). Resumption of spontaneous ovulatory cycles occurred in 43% of patients. In 57% an ovulation induction was needed. Conception in vivo occurred in 57%. There were no multiple pregnancies.

Our experience showed the feasibility of electrocautery of the ovarian capsule through transvaginal laparoscopy with results comparable with those obtained through standard laparoscopy.

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Evidence that CT scans can Influence Clinical Management of Encapsulating Peritoneal Sclerosis

Background

Encapsulating Peritoneal Sclerosis (EPS) is a rare but serious complication in peritoneal dialysis (PD) and is associated with duration of therapy. Current diagnosis is based upon clinical symptoms in combination with CT imaging and surgery.

Methods

Since 2004 to date we followed 84 patients that had been on PD for > 4 -5 years with 6-12 monthly CT scans. A total of 52 scans were performed in this group, with 21 patients receiving more than 1 scan.

Results

Of all 84 patients 37% died, 27% are now on haemodialysis, 17% remain on PD and 19% transplanted. In total 15% developed EPS .4/13 had pre-emptive surgery following routine CT scanning. There were 16% deaths from EPS. Of the 51 scans performed 71% were normal.

We have demonstrated that in some patients who developed EPS, CT scans detected progressive changes. Subsequently at the onset of gastro Intestinal symptoms, characteristic of EPS, pre-emptive surgery was implemented and outcome was improved.



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Anatomical position of different transoburator mesh-implants for anterior prolapse repair in women

Prospective and observational studies have shown that vaginal prolapse repair could be improved by using alloplastic meshes as tissue support. Therefore, a great number of meshes implanted via the transobuturator approach have been used in the last 2 years to treat same-site recurrence and stage 3 or 4 prolapse. The majority of these implant kits are composed of polypropylene, but they all differ in size and fixation. The aim of this cadaver study was to measure and compare the 4 main mesh products available on the German market with regard to their anatomical position in the pelvic floor after implantation.

To implant the 4 polypropylene meshes in the anterior compartment, one female pelvis was dissected medially by opening the retropubic space and visualize the entire endopelvic fascia attached to the arcus tendineus fascia pelvis(ATFP). After measuring the length of ATFP and interspinal distance, we implanted four different meshes using a transobuturator approach. We measured the distances between the introducer needles and the end position of the implant with regard to the landmarks of the pelvic floor. First, we implanted the Avaulta System, then the Perigee System. After that we used the Gynecare Prolift and the Seratom System.

The distance of the white line toward the ischial spine was 105mm and interspinal 131mm. The proximal fixation of the Avaulta was 20 mm distant to the spine and the lateral edge 10mm from the ATFP. The proximal edge was 20mm distant to the interspinal level. Perigee System was distant 25mm from the ischial spine and laterally 20mm. The proximal edge reached the interspinal level. The proximal fixation of Prolift was 10mm from the spine and the lateral edge touched the ATFP as well as the proximal edge the interspinal level. The Seratom is placed sacrospinous and the proximal edge and fixation are directly connected to the ischial spine.

Not all the implants reach the interspinal level, which is important for fixating the vaginal apex to stabilize defects in level I. With the exception of the Gynecare Prolift System, none of the other implants covered the lateral defect of the endopelvic fascia. The Seratom System might be the only product that repairs Level II and I defects because of the additional sacrospinous fixation. We do not know, however, whether the currently available products differ in terms of long-term efficiency or erosion rate.



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Topic : Adhesion Prevention

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BXL746, a VDR agonist, for the prevention of post-surgical adhesion formation

Post-surgical adhesion formation is a cause of significant morbidity. Preventive therapies could include reduction of fibrin deposition and inflammation. VDR agonists possess well known anti-inflammatory and fibrinolytic activities, that make BXL746 amenable to development for the prevention of PSA.

We have investigated the effect of BXL746 on fibrinolytic pathway and inflammation, in vitro on human mesothelial cell line and ex-vivo on mice during the formation of post-surgical adhesions. We tested the efficacy of BXL746, administered IP at the end of surgery, in mouse and rabbit models of PSA.

BXL746 reduces the secretion of inflammatory cytokines (IL-1beta, IL-6, IL-8) and increases tPA/PAI-1 ratio in vitro and ex-vivo. BXL746, administered IP at the end of surgery, is able to reduce post surgical adhesion formation in a dose dependent manner in mouse and DUH rabbit models.

Available data support the further development of the VDR agonist BXL746 in liquid formulation, administered IP at the end of surgery, for the preventive treatment of post-surgical adhesions.

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HIGH UTEROSACRAL LIGAMENT SUSPENSION COMPARED WITH

Objective: To compare efficacy and major complication of high uterosacral ligament suspense(HUSS) and Posterior Intravaginal Sling (P- IVS) for level one defect..

Methods: Prospective evaluation of 78 women with utrine or vault prolapse grade two greater. In 54 P-IVS was placed . HUSS was performed in 24 women In the P-IVS group 35 (65%) patient had anterior colporrhaphy and 50 (91%) had posterior colporrhaphy . In the HUSS group 23 (96%) patient had anterior colporrhaphy and 24 (100%) posterior colporrhaphy . The women had pre and post operative prolapsed quantification measurement, urinary and bowel symptoms assessment.

Results: Baseline characteristics, including age, parity, weight of the heaviest baby delivered, were not significantly deferent between the groups The median follow-up was 41 weeks (range 6-200) in the HUSS group and 42 weeks (range 6-168) in the

P- IVS group. The recurrence of apical prolapse beyond grade one was 5% with HUSS and 8% with post IVS . There was one (5%) ureteric injury that necessitate nephrostom placement in the HUSS group and two (10.5%) pelvic hematoma in the post. IVS group, one infected that necessitate antibiotic treatment and the other blood transfusion. Two (4%) tapes were excised because of extrusion.

Conclusion: The two technique have good anatomic results, the decision which of them to use should be based on patient decision regarding major complication.



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Peritoneum : Recto or Verso ?

Repair of peritoneal defects occurs from underlying mesenchyma. Trauma induces local suppression of peritoneal fibrinolysis promoting adhesions formation. No clear, neither effective recommendation exist nowadays to prevent adhesions formation. Incidence of adhesions formation in porcine model is high even after laparoscopic procedures.

We performed natural orifice transluminal endoscopic surgery on six pigs to explore the retroperitoneum. Accidental perforation of peritoneum occurred in 3 pigs. Adhesions were evaluated as follows : grade 0-4, where 0, no adhesion; 1, filmy avascular adhesions; 2, vascular adhesions; 3, cordlike fibrous adhesions; and 4, plain fibrous adhesions.

All pigs survived three weeks. There were no changes in feeding habits, neither signs of distress. On second look laparotomies, no adhesions were found in all pigs. On the peritoneal perforation site, we found fibrosis and thickening of the peritoneum with grade 0 adhesions. No diffuse retroperitoneal fibrosis, abscess or fluid collection were noted.

Peritoneal cicatrisation seems to be side specific. On the retroperitoneal side, the mesenchyma and local suppression of peritoneal fibrinolysis seem to react in a different manner to trauma than on the intraperitoneal side. This can help in some surgeries to prevent adhesions. More studies are mandatory to confirm this conclusion.

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Persistent pelvic pain induced by spinal arachnoid cysts mimicks symptoms of gynecological diseases

Persistent pelvic pain (PPP) is a common symptom of many gynecological conditions. It is difficult to establish the proper cause of this symptom and for this reason diagnostic laparoscopy, as well as imaging technologies are used. MRI was used to determine the cause of severe PPP in gynecological patients with complicated anamneses.

Initially, in this study, 984 gynecological patients with severe PPP were included. All patients were examined by clinical assays, Sonography and T1- and T2- weighted MR images (Hitachi AIRIS II, Japan, 0.35 Dø) in sagittal and axial projections. Finally, MRI data of 31 patients with spinal arachnoid cysts (SACs) were substantially analyzed.

Initially, pelvic inflammatory diseases in 893 patients, genital endometriosis in 73 patients and enlarged pelvic veins in 18 patients were considered as a cause of severe PPP. We found SACs in 31 patients by MRI and in these patients other causes of PPP were excluded. SACs were located in S1 – in 4, in S2 – in 20 and in S3 – in 7 cases. In 21 patients, SACs were complicated by vertebral degenerative dystrophic changes.

Using MRI in a complex of diagnostic facilities for gynecological patients with severe persistent pelvic pain is beneficial to determine the proper cause of this symptom. Severe persistent pelvic pain induced by spinal arachnoid cysts can mimick symptoms of gynecological diseases and it is difficult to properly visualize them by other diagnostic tools.



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Efficiency of Tachosil® to prevent post surgical adhesions development on female rat model. Study about the impact of the haemostatic sponge on uterine parenchyma

Post operative surgical adhesions in abdominal and pelvic surgery can have a major impact on patient's subsequent health (significant cause of female infertility, bowel obstruction, chronic pelvic pain and difficulties at the time of reoperation).

Despite the development of many surgical techniques and the use of several products to prevent or minimize the formation of adhesions following surgery, at least, 50 % of patients still develop significant adhesions.

TachoSil® is a haemostatic agent; under conditions of inadequate hemostasis, it can contribute to decrease adhesions development.

The study will be achieved on an animal model of sexually mature female rats randomly assigned to two different studying groups.

A standardized parietal peritoneum and uterine injury will be performed by laparoscopy. Group one, the control group, won't benefit from TachoSil® but from bipolar electrocoagulation of injured areas. Group two will benefit from a piece of TachoSil® which will cover the injured areas.

A second-look laparoscopy will be performed ten weeks after the initial surgery to evaluate post-operative adhesions.

The final procedure will be a hysterectomy with bilateral salpingo oophorectomy performed by laparotomy.

This study is based on 2 aims, first one is to evaluate the possible anti adhesions ability of TachoSil®, and second one is to investigate on a possible earlier effect of the fleece-bound sealing system on the uterine and ovarian parenchyma.

Detailed results about adhesions formation and the effect of TachoSil® on the uterus will be presented.

Evaluation of the ability of TachoSil® to prevent or reduce postoperative adhesions and its effect on the uterine parenchyma.



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SUCTION FORCE GENERATED BY ASPIRATION DEVICES CAUSES PERITONEAL TRAUMA

Peritoneal damage arises from many sources. To assess the effect of suction aspiration devices on intact peritoneum in the course of normal operating range during surgery an experiment was devised to analyze and measure the effect of negative pressure suction aspiration devices on intact porcine peritoneum as a potential source of peritoneal damage.

Five different suction aspiration devices were applied to intact porcine peritoneum for one, two or five (1, 2, or 5) seconds. The area of aspiration was biopsied and histologically evaluated. Suction aspiration devices were tested at negative pressures between 300 and 660 millimeters (mm) mercury or 5.8-12.76 pounds per square inch that is the normal operating range.

This normal range of operating circumstances caused peritoneal trauma. Peritoneal disruption reached a depth of five to eight mm diameter with sub-peritoneal hemorrhage. Gas evacuation rates ranged between 12-15 liters per minute or a velocity of 5.4-7.6 meters per second (m/s) for a 5 mm diameter device. Manufacturer recommended suction parameters would have resulted in velocities of 10.3-15.2 m/s.

Peritoneal contact with negative pressure suction aspiration devices traumatically dislodge and tear off intact peritoneum causing sub-peritoneal hemorrhage creating a condition for potential adhesion formation.



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Topic : Peritoneal physiology

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TISSUE GRASPERS CAUSE MESOTHELIAL ISCHEMIA AND HYPOXIA

Hypoxia and peritoneal damage are suspected as precursors to adhesions formation. The effect of tissue graspers on peritoneal tissue may cause ischemia. To analyze and measure the effect of laparoscopic grasping instruments on peritoneal tissue Doppler measurement was performed.

Doppler measurement of blood flow in peritoneal tissue when laparoscopic grasping instruments are used.

Traumatic ischemia was a universal occurrence with all devices evaluated. The mechanical advantage of grasping devices far exceeds measured tissue stiffness and its ability to resist ischemic compression.

Laparoscopic grasping instruments cause peritoneal ischemia. The force required to stabilize, pull, lift and move tissue by laparoscopic grasping instruments causes alteration in blood flow resulting in peritoneal hypoxia and ischemia.



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TISSUE GRASPERS CAUSE PERITONEAL DAMAGE

Surgical induced peritoneal trauma is associated with adhesion formation. To assess the tissue effect of tissue graspers on intact peritoneum and analyze and measure the effect histologically a porcine model was devised.

Peritoneal biopsy was obtained from sites of grasped peritoneum from each of the grasping devices analyzed using histologic methods.

Peritoneal damage was seen with all graspers. Tissue edges showed crush injury, edema, sub-peritoneal hemorrhage and loss of surface integrity.

Peritoneal trauma is caused by laparoscopic grasping instruments.



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TISSUE GRASPERS' FORCE CAUSES PERITONEAL DAMAGE BY CRUSH TRAUMA

Tissue graspers may contribute to peritoneal damage. To assess the grasping strength of laparoscopic instruments and determine their effect on mesothelial covered tissue an animal model was devised to analyze and measure grasping instruments force (crush strength), tissue deformation characteristics and histologic effect.

A strain gauge with force feedback capability as a thin film load cell or piezo-resistive sensors was incorporated into laparoscopic grasping devices to measure load pressure to measure laparoscopic grasping instrument force and deformation characteristics on tissue samples.

Grasp strength equaled crush strength for all instruments on all tissues tested. The force generated by the instruments tested surpassed the necessary parameters by a factor of three to five to stabilize, lift or move tissue.

Laparoscopic grasping instruments create excessive load pressures on tissues within their grasp. Laparoscopic graspers manipulate and handled tissue in a one crush strength fits all circumstance manner. Grasping strength of laparoscopic instruments should be modified to allow tissue stabilization without ischemic effects and with minimal tissue damage. The force required to stabilize, pull, lift and move tissue by laparoscopic grasping instruments is significantly less than that generated by currently available instruments.



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Topic : Peritoneal access for the 21st century (laparoscopy/notes...)

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Randomized Multicenter Controlled Study of Endoscopic and Surgical Closure of a Gastric NOTES Access Perforation in a Porcine Model.

A secure closure of the visceral perforation site is essential for NOTES procedures. We have developed a T-tag-based method for suturing through a regular flexible endoscope, making endolumenal closure of perforations possible. The aim of this study was to compare endoscopically sutured closure with closure via laparotomy in a randomized multi centre study.

Thirty-two pigs (18-38 kg) were used for the study. A standard gastric NOTES access perforation was created. After a diagnostic peritoneoscopy, the endoscope was withdrawn into the stomach and closure of the perforation was randomized to either endoscopic suturing, or laparotomy with surgical closure using running 4-0 monofilament suture. The abdominal wall was closed with a running 2-0 monofilament in the fascia and a 3-0 nonresorbable running suture in the skin. Recovery time and weight gain at 7 and 14 days were recorded. At necropsy, adhesions, abscesses or peritonitis were recognised.

Animals from the two groups had the same post-op recovery time and did not differ in post-op weight gain. 29/32 animals survived for 14 days. In the endoscopic group 1 pig died within 12 h post procedure in septicemia, and another was euthanized on day 7 due to rectal prolapse, both without signs of leakage. In the laparotomy group 1 pig was euthanized after 7 days due to incisional hernia, without signs of leakage. On day 14 there was significantly more distal adhesions in the laparotomized group (7/15) compared with the endoscopic group (1/14). Local adhesions at the perforation site were the same in both groups.

A gastric access perforation in order to perform a NOTES procedure can safely be closed endoscopically using endoscopic sutures. Animals in the endoscopic group had significantly less adhesions at autopsy and a tendency to recover faster post operatively, compared with the surgical group.



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Open Lysis of Adhesions (LOA) is More Effective in Decreasing Adhesion Reformation than Laparoscopic (Lap) LOA in a Rat Model

Up to 94% of patients undergoing open abdominal operations will develop adhesions, and a significant number of these patients will require a second operation for lysis of adhesions (LOA). Open LOA has traditionally been the treatment of choice for patients who have failed conservative management; however, minimally invasive procedures are increasingly being utilized. There are no studies to date that have compared adhesion reformation following open and laparoscopic LOA in humans. The aim of this study was to compare open and laparoscopic LOA on adhesion reformation in a rat model that was previously developed in this laboratory.

Intraabdominal adhesions were surgically induced in 48 rats using our ischemic button model. Seven days later, rats underwent laparoscopy (N=26) with carbon dioxide insufflation or laparotomy (N=22) to score and lyse adhesions. Twenty-four hours after LOA, 14 animals from each group (N=28) were sacrificed and peritoneal adhesion tissue and fluid were collected for analysis of tPA and PAI-1 mRNA and total fibrinolytic activity. The remaining 20 animals were sacrificed seven days after LOA and adhesion reformation was scored.

At the time of the first peritoneal exploration, $78 \pm 3.0\%$ of buttons formed adhesions. At the peritoneal re-exploration, all animals that underwent LOA had significantly fewer adhesions than at first look ($p < 0.05$); however, animals that underwent open LOA had 60% fewer reformed adhesions ($p < 0.05$) than the laparoscopic LOA group ($42 \pm 3.2\%$ vs. $17 \pm 6.3\%$). There was no significant difference in the tPA activity or tPA and PAI-1 mRNA levels between animals undergoing laparoscopic and open LOA.

In this model of adhesion formation/reformation, open LOA significantly prevented adhesion reformation compared to laparoscopic LOA, through a mechanism that does not appear to involve tPA. These data suggest that open LOA may be beneficial in the long-term management of adhesion related complications in patients with peritoneal adhesions requiring further surgery.



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MMP2 and MMP9 are upregulated following tumour-mesothelial interaction and promote tumour invasion via a PI3Kinase dependent pathway – an important step in the development of peritoneal metastasis?

Peritoneal metastasis is a significant occurrence in gastric cancer and is associated with a poor prognosis. A crucial step in its pathogenesis is the interaction between tumour and mesothelial cells. The matrix metalloproteinases (MMP) -2 and -9 are known to play an important role in tumour invasion. It is acknowledged that tumour-host interactions potentiate this process. The aim of this study was to investigate MMP changes following gastric cancer-mesothelial cell contact, the effects of these changes and the pathways responsible.

Human peritoneal mesothelial cells (HPMC) were co-cultured with HGC27 gastric cancer cells for varying time periods. Changes in MMP expression and activity for each cell type were analysed using quantitative RT-PCR and zymography. The role of the PI3kinase signalling-pathway was investigated using a PI3Kinase phosphorylation assay and by incorporating its selective inhibitor LY294002 into the co-culture system. Matrigel assays were used to measure invasion. Experiments were performed three times in triplicate. Kruskal-Wallis test was performed for multiple comparisons and differences between each group were analysed using Mann-Whitney U test.

MMP-2 and -9 activity in both cell lines was upregulated with tumour-mesothelial contact, as determined by zymography ($p=0.001$). This correlated with gene expression changes, with doubling of mmp2 gene expression in both cells following contact, and up to 20-fold increase in mmp9 gene expression in HPMC following tumour contact. PI3Kinase phosphorylation assay confirmed pathway activation. MMP-2 and -9 activity following tumour-mesothelial contact was attenuated by PI3Kinase inhibition ($p=0.017$). HGC27 cells in MMP-enriched co-culture media demonstrated increased matrigel invasion; this was attenuated in the presence of MMP inhibitor.

Tumour-Mesothelial contact results in upregulation of MMP-2 and MMP-9. Upregulation of MMP-2 and -9 appear to be dependent on PI3kinase signalling pathway activation. This increase in MMP-2 and MMP-9 activity appears to play an important role in promoting tumour invasion.



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A NEUROKININ 1 RECEPTOR ANTAGONIST (NK1RA) THAT REDUCES INTRAABDOMINAL ADHESIONS AUGMENTS THE ANTI-ADHESIVE EFFECTS OF A HYALURONIC ACID/CARBOXYMETHYLCELLULOSE (HA/CMC) ADHESION BARRIER IN RATS

Intraabdominal adhesions can be a significant cause of postoperative morbidity. Previous work from this laboratory has shown that an NK1RA significantly reduces adhesion formation in a rat model. HA/CMC (Septrafilm Adhesion Barrier® Genzyme), proven to reduce the incidence of adhesions in patients undergoing laparotomy, may have its efficacy limited to the location of the film, typically under the midline incision. The purpose of this study was to evaluate the anti-adhesion efficacy of the NK1RA (CJ-12,255; Pfizer) when administered in combination with HA/CMC in a rat model of adhesion formation.

Adhesions were induced in 36 rats using our ischemic button model. Rats received either IP saline, NK1RA, HA/CMC+saline, or HA/CMC+NK1RA at surgery. HA/CMC was applied unilaterally over half the buttons and the NK1RA was administered in a saline lavage. The rats were sacrificed at 7 days and adhesions scored as percent of buttons with formed adhesions. To evaluate peritoneal fibrinolytic activity, ischemic buttons were created and rats received IP NK1RA, bilateral HA/CMC+saline, or bilateral HA/CMC+NK1RA. Animals were sacrificed at 24 hours and peritoneal fluid was collected for analysis of tissue plasminogen activator (tPA) activity.

NK1RA reduced adhesions compared to controls ($80 \pm 8\%$ vs $20 \pm 4\%$; $p < 0.05$). HA/CMC also decreased adhesions from $75 \pm 8.3\%$ to $44 \pm 10.3\%$ ($p < 0.05$); however, this reduction was limited to buttons where HA/CMC was placed. NK1RA+HA/CMC increased the efficacy of HA/CMC, further reducing adhesions to $11 \pm 4.7\%$ compared to HA/CMC alone ($p < 0.05$). Adhesions were reduced by 45% on the non- HA/CMC side ($p < 0.05$). NK1RA increased peritoneal tPA activity 156% more than HA/CMC alone (11.8 ± 1.8 vs 4.6 ± 0.8 U/ml, $p < 0.05$). This increase was abrogated when NK1RA was administered in the presence of HA/CMC (5.9 ± 1.6 U/ml, $p < 0.05$ compared with NK1RA).

The efficacy of HA/CMC was significantly augmented by the addition of an NK1RA suggesting that further research is warranted to develop a biodegradable, barrier-based delivery system for more effective prevention of adhesions.



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Peritonectomy Is A Successful Treatment For Patients With Encapsulating Peritoneal Sclerosis (EPS) Following Renal Transplantation

Encapsulating peritoneal sclerosis (EPS) is an increasingly recognised complication of long term peritoneal dialysis (PD), associated with deposition of fibrous sheets which constrict and restrict the bowel. Surgical intervention has in several cases been associated in the past with high mortality.

Data was collected patients who developed EPS post renal transplantation in a single centre during 2004 to 2006. Diagnosis was based on clinical and radiological findings, with surgical confirmation.

11 patients developed EPS post transplant. 9 patients underwent peritonectomy and adhesiolysis, of whom 7 are now eating a normal diet. One patient underwent a repeat peritonectomy and is now almost symptom free. In this group of patients there has been one death.

Unlike previous reports of high surgical mortality up to 33% following peritonectomy in EPS patients, there has only been a 10% mortality in this group. The key to successful surgery is early semi-elective peritonectomy after adequate preparation.



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Peritoneum endometriotics implants and Adhesions treatment in large series of patients with 20 years of follow up.

Peritoneum is usually involved in pelvic endometriosis by adhesions, spot and deep infiltrating lesions. Different mechanisms have been suggests to explain diffusion disease and to threat implants. The aim of study is evaluate the extension of implants and adhesions in pelvis and the effects of their treatment at long term.

528 patients has been operated by laparoscopy in our service from 1985 to 2005 According to AFS patients were grouped in minimal, mild, moderate and severe. Adhesions were classified in filmy and dense; adnexal score was calculated and pelvic involvement was considered starting the operation. All data were reconsidered new one at the end of laparoscopy. However the peritoneal implants and lesions have been compared with Dysmenorrhoea, Dyspareunia and Chronic Pelvic Pain before and after surgery. Statistical analysis was realize using SPSS 16 for t Student test, parametric and non parametric analysis.

528 were patients operated in our department by Laparoscopy for endometriosis, chronic pelvic pain and infertility; 302 cases had a long term follow up, as 57,19 % of women. Mean age of patients was 32,5 year to which adhesions were classified in Moderate and Severe score. Peritoneal implants and adhesions appear not correlated with pain symptoms. Fertility and others results will be presented.

More frequently endometriotics implants are presents in the left side suggesting a physiological mechanism of circulating peritoneal fluid by which improve the possible contact among endometriotic cells and peritoneal surface. According to this hypothesis, our data confirm the different extension and gravity of adhesion in left side than the opposite.



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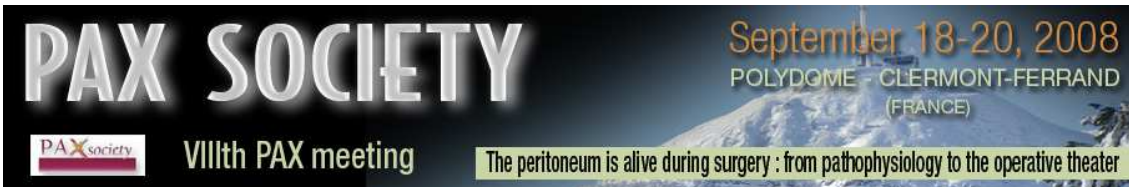
The adhesion production of propylene meshes that is applied with various substances and different mesh types

Incisional hernias are one of the common problems seen after abdominal surgical interventions. Incisional hernias those repaired by prosthetic materials may present with serious adhesions postoperatively. And these adhesions result in intestinal obstructions and enterocutaneous fistulas. These complications increase the morbidity. The aim of this study is to compare the adhesion production of propylene meshes that is applied with various substances and different mesh types at postoperative 30th. day and to investigate for the most proper mesh material.

In this study we used 70 Wistar Albino rats (180-220 gr). The rats are randomly divided into 7 groups. We entered into abdominal cavities with 3 cm midline incisions by using sterile techniques. We placed prolene mesh, indianoiled prolene mesh, vaselined prolene mesh, olive oiled prolene mesh, furacin treated prolene mesh and sepramesh to the 1st, 2nd, 3rd, 4th, 5th, 6th, and 7th groups respectively under the peritoneal layer. At each group, abdominal incisions of the rats are closed continuously by 2/0 silk. After 30 days, we sacrificed the rats and we made relaparotomy. Adhesions are graded according to Modified Diamond Scale.

When we compare the results of seven groups, in aspect of adhesions, adhesions were very few in dual and sepramesh groups but at high amounts in olive oiled prolene mesh group, in olive oiled prolene mesh group, adhesions were mostly dense and could be separated by sharp dissections. These adhesions were especially at the suture line. Adhesions those at the Indian oiled prolene mesh group were less than those at the prolene mesh group significantly.

From our point of view, to decrease the postoperative adhesions to the minimal levels, new studies and investigation of the new materials will be help.



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How to reduce peritoneal aggression during caesarean section: new question, old answer

Theoretically, avoiding the peritoneum opening during cesarean section (CS) would reduce peritoneal aggression and then further peritoneal adhesions formation. The aim of this study was to assess the feasibility and short outcome of exclusive extraperitoneal CS performed in the modern obstetric area.

Twenty-one pregnant women with planned CS after 37 weeks were prospectively enrolled in this study. CS was performed under locoregional anesthesia by a left laterovesical extraperitoneal route using a finger assisted dissection technique.

Twenty CS were successfully performed totally extraperitoneally. One attempt was converted to transperitoneal CS. Mean operative time and time to baby delivery were respectively 36.7 min (range 25-55) and 7,9 min (range 5-10). There was no maternal or fetal complication. Immediate outcome was excellent.

These results suggest that this technique of extraperitoneal CS is a safe and feasible option for planned cesarean delivery. The potential benefits of this surgical approach on postoperative pain, further adherence formation and infertility should be assessed in further studies.



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Adhesion prophylaxis with a rationally designed copolymer

Physical barriers are the only licensed adjuncts for adhesion prophylaxis in the USA and Europe. Here we investigate a rationally designed biomaterial, D,L-poly(lactide- $\hat{\mu}$ -caprolactone)trimethylenecarbonate (PCT copolymer), as an adhesion barrier in an animal model.

PCT copolymer was produced by melting of the monomers in organic solvents and subsequent processing by means of modified phase inversion and freeze drying. The glass transition point was modified from a previous version to facilitate laparoscopic application. In vitro cytotoxicity was assayed by fibroblast culture. In vivo adhesion prophylaxis was studied in a rat model involving standardized traumatization by electrocautery and suturing. The feasibility of laparoscopic application was assessed in 15 patients admitted for myomectomy.

PCT copolymer had no effect on the proliferation of cultured cells in vitro. The animal model showed that the quantity of adhesions covering the traumatized areas was significantly less in animals treated with PCT copolymer membrane (32%) than in untreated animals (79%) ($p < 0.001$). Laparoscopic application in humans was feasible.

Rationally designed biomaterials will increasingly impact in adhesion prophylaxis. These will allow qualitative advances such as the laparoscopic application of solid adhesion barriers and local elution of drugs.



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THE ABDOMINAL WALL LIFTING LAPAROSCOPIC SURGERY TO PREVENT THE INFLUENCE OF CO₂ GAS ON PERITONIUM

To discuss the advantages and doorstep of gas laparoscopist who will develop gasless laparoscopic surgery using the abdominal wall lifting to prevent the influence of CO₂ gas on peritoneum.

Thirty one cases of gasless laparoscopic surgery was performed using the abdominal wall lifting. The gasless laparoscopic surgeries were myomectomy 11 cases; eliminate ovarian cyst 9 cases, surgeries of fallopian tube 4 cases, monitoring hysteroscopic surgery 6 cases, laparoscopic adhesiolysis 1 case. Twenty nine cases were under general anesthesia as well as 2 cases epidural anesthesia. The abdominal wall of lower abdomen was lifted by abdominal wall lifting. Trocars were using in 16 cases and 15 cases using small incision with skin protect cover in which myoma and ovarian cyst can lift up and remove out while the abdominal was lay down.

Twenty seven cases were performed by gasless laparoscopy and 4 cases were completed under lower pneumoperitoneum pressure by complementary of CO₂. One case of ovarian cyst encountered severe adhesion was converted to laparotomy. Two cases suffered from pain of costal region post operation lasts two days. One case felt both shoulder pain and recovered spontaneously.

Gasless laparoscopy had the manipulation and advantages of both gas laparoscopy and laparotomy. Gasless laparoscopy is easier to handle for laparoscopists who were familiar with gas laparoscopy and to prevent the influence of CO₂ gas on peritonium.