Endoscopy: Revolution!

- Decreased Scars
  - Trauma
  - Pain
  - Hospital stay
  - Costs
REVELOLUTION ?

Mais !!

Adhesiolysis incidence : USA 1988 = 1994


Adhesion-related readmissions following gynaecological
laparoscopy or laparotomy in Scotland: an epidemiological
study of 24,046 patients

L.M.Jones1,2, R.J.S. Norwood3, D. Clark1, J.H. Hay1, A.R. Fidler1, A.D. Knight4
and A.M. Cross1 on behalf of the Surgical and Clinical Research (SCAR) Group

1The Royal Cornhill Hospital, 404 NCP, Stobcross Street, Glasgow G3 6SR, Naturogynaecology and Obstetrics Division.
2Laparoscopic Sterilisation Agency, Trowthorns Park, Heathfield Road, Basingstoke, Hampshire RG23 7OT, Division, Introduction (PVS), and Telford, Renfrewshire, Fergus, 
3To whom correspondence should be addressed. Email: sarah@swan.com

CONCLUSIONS: With the exception of laparoscopic sterilisations, open and laparoscopic gynaecological surgery are associated with comparable risk of adhesion-related readmissions.

But!!
Révolution ?

Open
difficult to change

Closed
easy to adapt

Other surgical specialities are interested ...

Intraoperative CO₂ insufflation can decrease the risk of surgical site infection

Mikael Persson *, Jan van der Linden **

* Division of Medical Engineering, Department of Laboratory Medicine, Karolinska Institute, Stockholm, Sweden
* Department of Cardiothoracic Surgery and Anesthesiology, Karolinska University Hospital, Karolinska Institute, SE 17176, Stockholm, Sweden

CO₂ as a tool for treatment of the peritoneum!

The potential use of carbon dioxide as a carrier gas for drug delivery into open wounds

Mikael Persson*, Jan van der Linden **

* Division of Medical Engineering, Department of Laboratory Medicine, Karolinska Institute, Stockholm, Sweden
* Department of Cardiothoracic Surgery and Anesthesiology, Karolinska University Hospital, Karolinska Institute, SE 17176, Stockholm, Sweden
PERITONEAL PHYSIOLOGY
AND
SURGERY

Peritoneal Membrane

Peritoneal Histology

1: cellules mésothéliales, 2: membrane basale, 3: Fibroblaste,
4: capillaires sanguins, 5: muscle, 6: fibres élastiques, 7 collagène
Peritoneal surface area

- It was recently measured in 10 non eviscerated cadavers
- The result was 14,323 ± 824 cm²
  - The visceral peritoneum represented 81.89 ± 0.99%
  - and the parietal peritoneum 18.11 ± 0.99%

Explained by the area of the diaphragm
Explained by the area of the mesentery

Which peritoneal surface is important?

- The area measured
- The area accounting for microvilli
- The area of the vessels which is essential for exchanges
- The volume of the inter cellular matrix
The Peritoneal Membrane

The peritoneal membrane

The peritoneal surface
Glycoaminoglycans

- The surface of the mesothelium is surrounded by a glycocalyx composed of Glycoaminoglycans (GAGs), Proteoglycans (PGs), and phospholipids, which together provide a slippery, non-adhesive layer that protects the serosal cavity from abrasion, infection, and tumor dissemination.
- The GAG and PG composition of the mesothelial glycocalyx remains to be fully defined.

Roles of Glycoaminoglycans

- PGs are major components, and they have diverse biologic functions, including binding and sequestration of growth factors and regulation of collagen fibrillogenesis.
- The control of peritoneal fibrosis:
  - Decorin has the ability to bind transforming growth factor-β (TGF-β) via its core protein, and in doing so, to neutralize the biologic activity of that growth factor.
  - Decorin has been shown to interact with collagen and to prevent collagen fibrillogenesis (18).
- Hyaluronan is a component of the mesothelial glycocalyx and protects the mesothelium from abrasion and adhesion.
- PGs and Mesothelial Permeability
- PG–Chemokine Interactions in the Peritoneum
Mesothelial « lubricant »

- Mesothelial cells secrete surface glycosaminoglycans, predominantly hyaluronan, which is assembled into hyaluronan-containing pericellular matrix "coats" around microvilli, protecting the cells from abrasive damage and infective agents.
- They also secrete phosphatidyl choline, the major constituent of the pulmonary surfactant (Mutsaers 2004).

- By binding to the glycocalyx which coats the microvilli, phospholipids may form a film… negatively charged microvilli attract positively charged phospholipid molecules with branched terminations creating the most efficient lubrication known in nature (Di Paolo and Sacchi 2000).

Peritoneal Lubricant ??

- Peritoneal cells have intracellular apparatus similar to those observed in pneumocytes.
- Peritoneal surface is hydrophobic.
- Phosphatidyl choline is found in the fluid recovered at the end of peritoneal dialysis.

Hydrophobicity of Peritoneal Tissues in the Rat.

<table>
<thead>
<tr>
<th>Peritoneal tissue</th>
<th>Water contact angles (degrees)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mesentery</td>
<td>0°</td>
</tr>
<tr>
<td>Peritoneal pouches</td>
<td>36 ± 7</td>
</tr>
<tr>
<td>Visceral peritoneum</td>
<td>16°</td>
</tr>
<tr>
<td>Small intestine</td>
<td>18°</td>
</tr>
<tr>
<td>Large intestine</td>
<td>16°</td>
</tr>
<tr>
<td>Bladder</td>
<td>41 ± 6</td>
</tr>
<tr>
<td>Liver</td>
<td>45 ± 8</td>
</tr>
<tr>
<td>Spleen</td>
<td>49 ± 7</td>
</tr>
<tr>
<td>Stomach</td>
<td>54 ± 9°</td>
</tr>
<tr>
<td>Kidney</td>
<td>65 ± 9°</td>
</tr>
</tbody>
</table>

Peritoneal tissues involved in absorptive and exchange functions and requiring lubrication are more hydrophobic than tissues with more important absorptive and protective functions.
Blue Test from « Manhès » !!

Mesothelial Cells
Les Cellules Mésothéliales

• 1 assise de cellules,
  • de 25 à 40 microns diamètre
  • porteuses microvillosités et de cils qui augmentent la surface d'échange
  • de forme complexe à contour géographiques

Histology

• Slowly growing tissue, it is estimated that only 0,16 to 0,5% of the cells are in mitosis at the same time

• This percentage increases to 30 and even 80% in an area traumatized 48 hours before.

Trois types de cellule

• On distingue trois types de cellule en fonction des zones
  • des cellules aplaties dont l'épaisseur (2 à 3 µ) augmente dans la région nucléaire, (péritoine pariétal, diaphragme, mésentère)
  • des cellules cubiques de 12 à 15µ d’épaisseur qui sont numériquement moins nombreuses (ovaires, foie, rate, îlots de Ranvier, en périphérie des stomas, en bordure des zones péritonéales traumatiques)
  • des cellules intermédiaires entre les deux types
2 main morphologic types of cells

<table>
<thead>
<tr>
<th>Epidermoid</th>
<th>Cubiques</th>
</tr>
</thead>
<tbody>
<tr>
<td>Noyau</td>
<td>Ovoid</td>
</tr>
<tr>
<td>Mitochondries</td>
<td>rare</td>
</tr>
<tr>
<td>REG</td>
<td>+</td>
</tr>
<tr>
<td>Golgi</td>
<td>+</td>
</tr>
<tr>
<td>Microtubules</td>
<td>+</td>
</tr>
<tr>
<td>Microfilaments</td>
<td>+</td>
</tr>
</tbody>
</table>

Microvilli

- The luminal surface of mesothelial cells has numerous microvilli, which vary in length, density and shape.
- These microvilli increase the mesothelial surface area up to 40m².
- Microvilli protect the delicate mesothelial surface from frictional injury by entrapping water, serous exudates, and phospholipids which act as lubricants for the cells.

Microvilli of the mesentery
Microvilli

- The density of microvilli depends on the area studied
  - ~230 /µ on the bladder
  - ~540 /µ on the spleen
  - Sometimes absent on the parietal and the diaphragmatic peritoneum (Di Paolo 2000)

- Most importantly, ultrastructural changes on the surface of the cells clearly demonstrate that microvilli are dynamic structures.

Mesothelial Microvilli

- The concentration of microvilli varies under different physiological and pathological conditions
- The concentration of microvilli formed on junctional plasmalemma was greater than on peripheral, which in turn was greater than that on perinuclear plasmalemma (P<0.05; Fig. 2).

Cilia

- Mesothelial cells also possess cilia which are 5 times longer than microvilli
- Their function is not known but
- Primary cilia may have a sensory function capable of detecting subtle changes in the composition of the serosal fluid including paracrine and hormonal regulators released into the fluid. The primary cilium is strategically placed to mediate a rapid cellular response given its close association with biosynthetic organelles.

Bird SD Cell Biol Int 2004
Conclusions: The study demonstrated that the morphologic integrity of the rat peritoneum is not disturbed when CO2 or helium is used for insufflation combined with the intraperitoneal injection of carcinoma cells. Pneumoperitoneum therefore probably is not the condition causing peritoneal changes that favor intraperitoneal tumor growth.

Differences ??

The model is essential !!
Animals and methods

- Induction: Isoflurane
- Videoendoscopic endotracheal intubation – (rigid 2 mm endoscope)

Animals and methods

- Analgesia: derivative of morphine (sufentanil)
- Anesthesia: curarisation (vecuronium bromide)
- Homeothermic blanket system, rectal probe
- Mechanical ventilator
- Adapted to the type of surgery:
  - Tidal volume (200 µl)
  - Strokes per minute (250: laparoscopy; 220 laparotomy, control)
- Values delimited in a preliminary study to obtain PCO2 : 25-35 mmHg and pH : 7.3-7.4

Animals and methods

- CO2 pneumoperitoneum, two catheters: one for insufflation, one connected to a water valve
- Laparotomy: 3 cm abdominal incision
- After 1 hour: Carotid blood sample were analysed to obtain PaO2, PaCO2 and pH
**Arterial blood gas analysis**

*In Mice without intubation*

<table>
<thead>
<tr>
<th>Control</th>
<th>CO2 Pneumoperitoneum 2mmHg (n=5)</th>
<th>CO2 Pneumoperitoneum 8 mmHg (n=5)</th>
<th>Laparotomy (n=5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PaO2 (mmHg)</td>
<td>101.3 ± 5.2</td>
<td>107.2 ± 2.0</td>
<td>78.2 ± 17.7</td>
</tr>
<tr>
<td>PaCO2 (mmHg)</td>
<td>36.2 ± 3.5</td>
<td>41.7 ± 2.3</td>
<td>61.8 ± 4.25</td>
</tr>
<tr>
<td>pH</td>
<td>7.374 ± 0.041</td>
<td>7.260 ± 0.012</td>
<td>7.155 ± 0.027</td>
</tr>
</tbody>
</table>

Data are mean ± SEM

Normal value of PaCO2 in mice: 25-35 mmHg

---

**Arterial blood gas analysis**

*In Mice with intubation*

<table>
<thead>
<tr>
<th>Control</th>
<th>CO2 Pneumoperitoneum 2mmHg (n=5)</th>
<th>CO2 Pneumoperitoneum 8 mmHg (n=5)</th>
<th>Laparotomy (n=5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PaO2 (mmHg)</td>
<td>106.6 ± 4.2</td>
<td>106.0 ± 3.2</td>
<td>112.2 ± 3.6</td>
</tr>
<tr>
<td>PaCO2 (mmHg)</td>
<td>26.8 ± 2.9</td>
<td>34.2 ± 2.3</td>
<td>32.2 ± 3.6</td>
</tr>
<tr>
<td>pH</td>
<td>7.379 ± 0.037</td>
<td>7.342 ± 0.023</td>
<td>7.269 ± 0.041</td>
</tr>
</tbody>
</table>

Data are mean ± SEM

Normal value of PaCO2 in mice: 25-35 mmHg

---

**Results: Peritoneum Dissemination score**

Non ventilated animals

Ventilated animals

P<0.004
Conclusions

- An adapted pressure must be used (further hemodynamics studies are necessary)
- In studies with no CRS, effect of pneumopertoneum might be reconsidered
- CRS is required for operative and post-operative studies in animals

Humidification

- Meta analysis are in favour of humidification


- Conclusions. Heated-humidified CO2 insufflation results in significantly less hypothermia, less peritoneal damage, and decreased adhesion formation as compared with cold-dry CO2 insufflation.
Mesothelial stem cells ?!

Potentiel fibroblastique

Fig. 3. Messenger RNA probe (A) and fibroblast marker (B) expression in mesothelial cells (EGF, vimentine), and fibroblasts (PDGF, IL-1β).

Dog peritoneal and pleural cavities as bioreactors to grow autologous vascular grafts

Wai-Lung Chan, MBBS,* Graeme B. Campbell, PhD,* Neil Caplice, MBBS, PhD,*
Amjad Mahamoodi, MD,* Cola L. Berry, MD,* Anita C. Thomas, MD,* Michael B. Bennett, PhD,* and
Julie H. Campbell, PhD,* Boston, Australia, and Kansas, USA

Objective: The purpose of this study was to grow “artiﬁcial blood vessels” for autologous transplantation in arterial reconstruction grids in a large animal model (dogs).

Methods: A total of 10 canines were used. Each dog was anesthetized, intubated, and the peritoneal or pleural cavity of dogs was exposed to the skin incision techniques, and intubated at one side and to the wall with a ﬂexible tube. After 5 weeks the tubes and their tissue caps were harvested, and the meniscus was discarded. The wall of biopsy tissues was immediately labeled 1, 2, 3, 4, 5, and 6, respectively, throughout the length, and consisted of multiple layers of mesothelial and mesothelial cells with a single layer of mesothelial. The mesothelial network was covered with a layer of mesothelial, and mesothelial cells. The bioreactor was then divided into sections, and mesothelial cells, bioreactor, and mesothelial cells were placed in a bioreactor. The mesothelial network was then placed in a bioreactor. At harvest, the harvested menisci were ﬁxed with solutions that contained for 1 week. After 1 week, the menisci were stained with antibodies and immunohistochemistry, and the mesothelial network was covered with a bioreactor. The results of these experiments are shown here.
B CELL Migration in the PERITONEUM

Barberich et al J Immunol 2008

FIGURE 7. Schematic presentation of B2 cell migration into the PerC and ovary from the peritoneum under inflammatory conditions. B2 cells enter the PerC via two independent routes. In one, integrin-mediated directed migration of B1 cells from the circulation into the PerC and 2 blood-borne B2 cells enter posteriorally upon the B1 subset MADCAM-1 interaction and subsequently might transmigrate into the PerC. Inside the PerC, the majority of H1 cells are retained in the compartment by α4 integrin-dependent adhesion to the local matrix. This interaction limits the pool of nonhematopoietic resident B2 cells that can exit this compartment in a β2 integrin-mediated mechanism via the draining lymph nodes or alternatively enter central nodes upon the preserved role. Dashed bars indicate potential regulatory events that have not yet been experimentally shown.

Mesothelial Cells

- Les cellules mésothéliales secrètent
  - Prostaglandines E2 and I2
  - Cytokines (IL1, IL6, TGFβ, EGF, VEGF, G-CSF, M-CSF)
  - Chemokines (IL8, MCP-1)
  - Composants de la matrice extracellulaire (Fibronectine, Laminine, collagène de Type III ,acide hyaluronique [récepteur CD44])
  - Protéines de l’hémostase (tPA, PAI1)
  - Phosphatidyl choline...........
Mesothelial Cells

- Phagocytosis
- Antigen presentation
- HLA DR expression induced by après traitement interferon gamma
- IL 15 secretion (activateur de cellules T)

The mesothelium contributes to:

- The initial response of the peritoneum to infection
- The amplification of this response
- The recruitment of leucocytes
- The control and the resolution of inflammation
- The control of peritoneal fibrinolysis
- The control of peritoneal homeostasis and maintenance of peritoneal membrane structure and function.

Stoma

Fig. 3: Scanning electron micrograph of mesentery. Two stoma can be seen in the micrograph, one of them containing a red blood cell. The mesothelium covers the margins of the stoma. Bar, 10 μm. (A) Transmission electron micrograph of the specimen shown in (C) showing the mesothelial cell in the middle of the stoma. The mesothelial cells cover the inner surface of the stoma from the margins of the opening. The mesothelial cells are closely apposed to the inner surface. Bar, 0.5 μm.

E.R. TITTARELLI AND R.G. CARR

November 10

November 10

November 10
Les stomas diaphragmatiques

- Situés à la jonction de 3 à 5 cellules mésothéliales
- Plus fréquents sur la coupole diaphragmatique droite
- Leur diamètre varie de 4 à 10 microns mais varie en fonction des circonstances (tension du diaphragme, pression intrapéritonéale, circonstance pathologique) en raison de la présence de filaments contractiles dans les cellules mésothéliales
- Ces stomas mettent en communication la cavité péritonéale avec le système lymphatique, les membranes basales du mésothélium et de l’endothélium lymphatique sont discontinues à ce niveau.
- Les lacunes lymphatiques communiquent avec les lymphatiques sous-pléuraux.
- Des bactéries injectées dans le péritoine de chien sont retrouvées dans le canal thoracique moins de 6 minutes après l’injection.

Plus en détail

- Le passage de globules rouges et de particules diverses a été confirmé par de nombreux auteurs.
- Le nombre et le diamètre des stomas dépend des circonstances. Certains auteurs ne les observés qu’après l’injection intrapéritonéale de globules rouges. (a)
- Pour certains le diamètre se modifierait avec la respiration.
- Pour de nombreux auteurs ces « orifices » sont clairement identifiables en microscope à balayage et plus difficilement en microscopie électronique.
- De même la continuité directe avec le système lymphatique n’est pas toujours confirmée ou aurait des modalités variables en fonction des sites péritoneaux.

Lymphatiques du diaphragme
There stoma in other areas

- omentum
- anterior abdominal wall
- on the liver (rat)
- pelvis particularly on the broad ligament

Omentum

- No spontaneous movements
- Milky spots are concentrations of immune cells, main origin of peritoneal macrophages and sites of lymphocytes differentiation
- Omentectomy induces significant changes in peritoneal cellular population
Gerber SA, Rybakko YY, Bigelow CE, Lugade AA, Foster TH, Frelinger JG, Lord EM.
Preferential attachment of peritoneal tumor metastases to omental immune aggregates and possible role of a unique vascular microenvironment in metastatic survival and growth.
Insufficient ability of omental milky spots to prevent peritoneal tumor outgrowth supports onchoectomy in minimal residual disease.

Omentectomy resulted in reduced intra-abdominal tumor load, which was completely attributable to the absence of the omentum, as tumor development did not differ on other sites.

Conclusion: Since the ability of omental milky spots is, even in MRD, insufficient to prevent intra-abdominal tumor outgrowth, onchoectomy, which reduces tumor load, is recommended in surgical treatment of intra-abdominal tumors that are prone to disseminate intraperitoneally.
Tissue oxygenation is one of the most important determinants in wound healing, adhesion formation, tumor growth.
Hypoxemia and tumor invasiveness

This effect is likely induced by hypoxemia, it is abolished by an MMP inhibitor.

Peritoneal tissue oxygen tension

- Peritoneal tissue oxygen tension was measured using a polarographic oxygen electrode placed in the retroperitoneal space using a 16 gauge intravenous catheter.
- The PitO2 level were monitored continuously.
- Following the trauma of implantation, the intraoperative values were averaged across the last 30 minutes of the procedure.
Peritoneal tissue oxygen tension (PitO2)
in mice with controlled respiratory support

<table>
<thead>
<tr>
<th></th>
<th>Control (anesthesia alone)</th>
<th>CO2 pneumoperitoneum 2mmHg (n=5)</th>
<th>CO2 pneumoperitoneum 8 mmHg (n=5)</th>
<th>Laparotomy (n=5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PaO2 (mmHg)</td>
<td>106.0 ± 4.2</td>
<td>106.0 ± 3.2</td>
<td>112.2 ± 3.6</td>
<td>105.4 ± 4.4</td>
</tr>
<tr>
<td>PitO2 (mmHg)</td>
<td>45.0 ± 3.5</td>
<td>104.2 ± 7.8</td>
<td>64.2 ± 9.6</td>
<td>49.8 ± 15.0</td>
</tr>
</tbody>
</table>

Data are mean ± SEM

\( p<0.05 \) vs Control, CO2 pneumoperitoneum at high IPP, Laparotomy

Peritoneal tissue oxygen tension (3)

- To understand whether this result is related to pressure or to CO2
- Two groups of 3 animal with controlled respiratory support
  - 3 with CO2
  - 3 with air
  - Each animal had
    - anesthesia for 1 hour,
    - pneumoperitoneum for 1 hour
    - and laparotomy for 1 hour
Comments

• Surprising result

• P\textsubscript{AO2} depends on the following factors
  – Delivery of oxygen from the lung to the tissue
  – Transport of oxygen from blood to the tissue
  – Oxygen consumption in the tissue

• The peritoneum pH is very low even in animal with control respiratory system (Hanly et al 2005), so CO\textsubscript{2} pneumoperitoneum could increase the transport of oxygen through the Bohr effect

• In ventilated pigs, a CO\textsubscript{2} pneumoperitoneum 5 - 12 mmHg increases peritoneal blood flow and this may increase the delivery of oxygen to the tissue

• This has to be confirmed at the cellular and the molecular level.

Which pressure is acceptable in a mouse model?

CO\textsubscript{2} pneumoperitoneum, intraperitoneal pressure and peritoneal tissue hypoxia: A mouse study with controlled respiratory support

• BACKGROUND: Hypoxia has many adverse effects on biological systems. The aim of this study was to investigate whether the surgical peritoneal environment is hypoxic in a mouse model.
Methods

Mice were divided into five groups:
- anesthesia alone,
- laparotomy,
- CO$_2$ pneumoperitoneum at intraperitoneal pressures (IPP)
  - 2 mmHg,
  - 8 mmHg
  - 15 mmHg.

Over the course of each experiment, the peritoneal tissue oxygen tension (PiO$_2$) was continuously monitored.

Methods

- Peritoneal tissue oxygen tension
- A 16 gauge intravenous catheter was inserted into the retroperitoneal space (beneath the peritoneal membrane) from the left lateral upper quadrant to left lateral lower quadrant, just before surgical procedures. A polarographic oxygen electrode (Integra Neuroscience, Sophia Antipolis, France) was inserted through the catheter and placed in the retroperitoneal space near the left lateral abdominal mammary gland to measure the peritoneal tissue oxygen tension (PiO$_2$). The PiO$_2$ was continuously monitored on a LICOX CMP monitor (CC1.P1, oxygen sensitive part diameter: 0.65mm, oxygen sensitive area: 18mm$^2$, Integra Neuroscience) during procedures. To obtain reliable PiO$_2$ readings, the tissue was allowed to stabilize following the microtrauma of implantation and the intraoperative values were averaged across the last 30 minutes of the procedure in each mouse. The resulting values were then averaged among the mice in each group for protocol 1. This is a well-established method for evaluating tissue-oxygen partial pressure (Akca et al., 1999; Greif et al., 2000)

Methods

- Peritoneal hypoxia at the cellular level was studied using Pimonidazole
  - Pimonidazole administration
  - Pimonidazole hydrochloride (Hydroxyprobe-1; Natural Pharmaceuticals International Inc., Research Triangle Park, NC; concentration 1.0 mg/100 ml in 0.9% saline) was administered at 70 mg/kg.
Results: PTIO2

A, C, D, F: No immunostaining was detected in either the mesothelial or stromal cells. B: Immunostaining was detected in both mesothelial and stromal cells. E: Immunostaining was detected in stromal cells. Mesothelial cells were not detected because of the detachment (Arrows).

Preliminary clinical data

Pit02

FiO2: 0.4

FiO2: 1.0

FiO2: 1.8

FiO2: 0.4

normal non traumatized

traumatized
Effects of supplemental perioperative oxygen on post-operative abdominal wound adhesions in a mouse laparotomy model with controlled respiratory support

Saëska Matsuoka1,2, Michel Casas1,2, Jean-Eloi Beato1,2, Claude Dubois3, Jean-Luc Puey1,2 and Gérard Magi1

1 Université de Nancy, EA 235, Faculté de Médecine, Centre d'Études des Récipients Intravasculaires (CERI), C.N.R.S. 228/Boulevard de l’Hôpital, 54000 Nancy, France; 2 INSERM U944, centre de recherche, hôpital de la Pitié-Salpétrière, 75730 Paris, France; 3 Université de Nancy, EA 136, Faculté de Médecine, Centre d'Études des Récipients Intravasculaires (CERI), C.N.R.S. 228/Boulevard de l’Hôpital, 54000 Nancy, France.

BACKGROUND: Post-operative adhesions formation is a major clinical problem. These adhesions are one of the most frequent determinants in abdominal surgery. The objective of the study was to investigate whether a high oxygen-perioperative oxygen could reduce post-operative adhesions formation through inducing the permeability of new mesothelial (PMO) in a mouse model. 10 mice were randomly divided into two groups: Group 1 (n = 5) received postoperative intraperitoneal saline injection and Group 2 (n = 5) received postoperative intraperitoneal saline injection plus 1% oxygen. The medium cell density was measured on the day 10 post-operation, the day 30 post-operation and the day 60 post-operation. The cell density was measured on day 10 and day 30 post-operation, and the cell density was significantly higher in the Group 1 than in the Group 2 (P < 0.05). The cell density was measured on day 30 post-operation, and the cell density was significantly reduced in the Group 2 compared to Group 1 (P < 0.05) and P < 0.001, respectively.

Model of ovarian rupture

ID 8, Mouse epithelial ovarian cancer cell line
Dr. K. Roby, University of Kansas Medical Center (Carcinogenesis 2000)

1 x 10^6 cells

intrapertoneal

immunocompetents C57BL/6 8 weeks, mice.
**Results: Peritoneum Dissemination score**

The role of pressure was confirmed using pathologic examination of the implants.

Invasion: negative

Muscle tissues: free of cancer cells
Invasion: Positive Minimal

Muscle tissues: invasive cancer cells

Invasive: Positive Massive

The structure of the muscle is destroyed

Results: Peritoneum

Invasion of cells into muscle tissues

<table>
<thead>
<tr>
<th>Incidence (%)</th>
<th>Laparotomy 8 mmHg</th>
<th>2 mmHg Anesthesia alone</th>
</tr>
</thead>
<tbody>
<tr>
<td>P&lt;0.002</td>
<td>100</td>
<td>80</td>
</tr>
<tr>
<td>P=0.007</td>
<td>80</td>
<td>40</td>
</tr>
<tr>
<td>P&lt;0.03</td>
<td>40</td>
<td>20</td>
</tr>
<tr>
<td>P=0.007</td>
<td>20</td>
<td>10</td>
</tr>
</tbody>
</table>
Liquide péritonal:

Circulation

* Circulation des liquides dans la cavité péritonéale

- Blocage
- Passage
Circulation des liquides dans la cavité péritonéale

Sites des biopsies

Dissemination to the Diaphragm

Table 5: Results of dissemination score on the diaphragm

<table>
<thead>
<tr>
<th></th>
<th>Laparotomy</th>
<th>High IPP</th>
<th>Low IPP</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 days</td>
<td>0.0 ± 0.0</td>
<td>0.0 ± 0.0</td>
<td>0.0 ± 0.0</td>
<td>1.0 ± 0.0</td>
</tr>
<tr>
<td>POD 7</td>
<td>3.5 ± 0.5</td>
<td>1.5 ± 0.7</td>
<td>0.5 ± 0.5</td>
<td>0.0 ± 0.0</td>
</tr>
<tr>
<td>POD 14</td>
<td>2.0 ± 0.5</td>
<td>1.0 ± 0.3</td>
<td>0.5 ± 0.5</td>
<td>0.0 ± 0.0</td>
</tr>
<tr>
<td>POD 42</td>
<td>3.0 ± 0.6</td>
<td>2.5 ± 1.0</td>
<td>1.5 ± 0.5</td>
<td>0.5 ± 0.5</td>
</tr>
</tbody>
</table>

IPP: intraperitoneal pressure; POD: postoperative day
* All data are expressed as mean ± standard error of the mean
* * p < 0.01 vs laparotomy; p < 0.001 vs high IPP, low IPP
* # p < 0.001 vs Laparotomy, control
* ! p < 0.001 vs laparotomy; p < 0.01 vs control

Dissemination to the Bowel

Table 6: Dissemination to the bowel

<table>
<thead>
<tr>
<th></th>
<th>Laparotomy</th>
<th>High IPP</th>
<th>Low IPP</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence (%)</td>
<td>100*</td>
<td>87.5</td>
<td>62.5</td>
<td>37.5</td>
</tr>
<tr>
<td>Dissemination score</td>
<td>5.0 ± 0.0*</td>
<td>1.62 ± 0.32</td>
<td>1.38 ± 0.42</td>
<td>0.88 ± 0.44</td>
</tr>
</tbody>
</table>

IPP: intraperitoneal pressure
* * p < 0.01 vs controls
* * * Data are mean ± standard error of the mean
* * * * p < 0.0001 vs high IPP, low IPP, and control
Dissemination to the liver

**Table 7: Dissemination to the liver**

<table>
<thead>
<tr>
<th>Procedure/Incidence</th>
<th>Laparotomy (n = 8)</th>
<th>High IPP (n = 8)</th>
<th>Low IPP (n = 8)</th>
<th>Control (n = 8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence (%)</td>
<td>100*</td>
<td>12.5</td>
<td>57.5</td>
<td>12.5</td>
</tr>
<tr>
<td>Dissemination score*</td>
<td>3.5 ± 0.59</td>
<td>0.13 ± 0.13</td>
<td>0.49 ± 0.13</td>
<td>0.13 ± 0.13</td>
</tr>
</tbody>
</table>

* p < 0.01 vs high IPP; p < 0.03 vs low IPP, control
* Data are mean ± standard error of the mean
* p < 0.0001 vs high IPP, low IPP, and control

Molecular analysis

Peritoneal Carcinomatosis Model
# Materials and Methods

<table>
<thead>
<tr>
<th>Preimplanted tumor cells</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Intraperitoneal Injection</td>
<td>7 days before randomization</td>
</tr>
<tr>
<td>Surgery</td>
<td>Randomisation: Laparotomy, Low Pressure Pneumoperitoneum (LPP), High PP (HPP), Anesthesia</td>
</tr>
<tr>
<td>Evaluation</td>
<td>POD 1-2-7-14</td>
</tr>
</tbody>
</table>

## Post operative

**Dissemination scores**

![Intramuscular Invasion Chart]

<table>
<thead>
<tr>
<th>Laparotomy</th>
<th>HPP</th>
<th>LPP</th>
<th>Anesthesia</th>
</tr>
</thead>
<tbody>
<tr>
<td>POD14</td>
<td>100</td>
<td>90</td>
<td>80</td>
</tr>
</tbody>
</table>
Conclusion

- Surgical environment has a huge influence on peritoneal dissemination
- On a preimplanted ovarian cancer model, laparoscopy performed under low pressures, could create an optimal environment to minimize peritoneal dissemination
- On a preimplanted tumor model, surgical environment has no influence, either on tumor growth or on trocar site metastases incidence

Impact of the Surgical Peritoneal Environment on Pre-implanted Tumors on a Molecular Level: A Syngeneic Mouse Model

Sachiko Matsuzaki, M.D.§,十分 Anne Sophie Amse, M.D.§,十分 Georges Haga, M.D.§,十分 and Michel Cariou, M.D.§,十分

Université Clermont-Ferrand I, Centre d’Référence on les Maladies Pathogènes Environnementales (CRMPH, Clermont-Ferrand, France), and INSU (Institut National de la Santé et de la Recherche Médicale, Clermont-Ferrand, France)
Conclusion

• **Early post-operative windows** has been underlined.
• Peri-operative treatments could be an interesting strategy in oncologic surgery and need to be assessed

Demain

• L’image va continuer de progresser; l’accès au péritoine évoluera...
• « L’atmosphère » chirurgicale va devenir un traitement ou permettre des traitements.
• Ceux qui travaillent dans des milieux ouverts et avec leur yeux vont devoir changer leur habitudes .......
• Mais pour utiliser au mieux cet environnement endoscopique il faut en comprendre les effets sur les tissus normaux et en situation pathologique.
THE REVOLUTION IS STILL AHEAD!!