MSRM International Meeting

"ENDOMETRIOSIS
Current Management and Future Trends"

21 - 23 October 2011
Gran Melia, Vathi, Agios Nikolaos
Crete - Greece

Under the auspices of the University of Crete

Final Programme & Book of Abstracts
Contents

COMMITTEES - FACULTY .............................................................................................................2

PRESIDENTS' MESSAGE ............................................................................................................3

SCIENTIFIC PROGRAMME ........................................................................................................4-7

GENERAL INFORMATION .........................................................................................................8-10

ACKNOWLEDGEMENTS ..........................................................................................................11

ORAL PRESENTATIONS ..........................................................................................................13-19

INVITED SPEAKERS’ ABSTRACTS ..........................................................................................21-39
## Committees

### Meeting Chairman
Professor: A. Makrigiannakis, MD, PhD

### MSRM Executive Committee

<table>
<thead>
<tr>
<th>Position</th>
<th>Name</th>
<th>Country</th>
</tr>
</thead>
<tbody>
<tr>
<td>Honorary President</td>
<td>H. Sallam</td>
<td>Egypt</td>
</tr>
<tr>
<td>Chairman</td>
<td>P. Inaudi</td>
<td>Italy</td>
</tr>
<tr>
<td>General Secretary</td>
<td>K. Mahmoud</td>
<td>Tunisia</td>
</tr>
<tr>
<td>Treasurer</td>
<td>I. Messinis</td>
<td>Greece</td>
</tr>
<tr>
<td>Executive Members</td>
<td>R. Ron-El</td>
<td>Israel</td>
</tr>
<tr>
<td></td>
<td>L. Nardo</td>
<td>UK</td>
</tr>
<tr>
<td></td>
<td>A. Demirod</td>
<td>Turkey</td>
</tr>
<tr>
<td></td>
<td>T. Motrenko</td>
<td>Montenegro</td>
</tr>
<tr>
<td></td>
<td>A. Watrelot</td>
<td>France</td>
</tr>
</tbody>
</table>

### Local Organizing Committee

<table>
<thead>
<tr>
<th>Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>M. Alexiou</td>
</tr>
<tr>
<td>M. Asmarianaki</td>
</tr>
<tr>
<td>P. Drakakis</td>
</tr>
<tr>
<td>A. Gravanis</td>
</tr>
<tr>
<td>S. Kalantaridou</td>
</tr>
<tr>
<td>T. Karagiozis</td>
</tr>
<tr>
<td>M. Karamouti</td>
</tr>
<tr>
<td>P. Kondilis</td>
</tr>
<tr>
<td>S. Kourletakis</td>
</tr>
<tr>
<td>D. Loutradis</td>
</tr>
<tr>
<td>G. Manidakis</td>
</tr>
<tr>
<td>M. Marazaki</td>
</tr>
<tr>
<td>A. Margioris</td>
</tr>
<tr>
<td>N. Martavantzis</td>
</tr>
<tr>
<td>S. Mavrogianaki</td>
</tr>
<tr>
<td>I. Messinis</td>
</tr>
<tr>
<td>N. Paikopoulos</td>
</tr>
<tr>
<td>M. Parisis</td>
</tr>
<tr>
<td>M. Plekanos</td>
</tr>
<tr>
<td>G. Petsas</td>
</tr>
<tr>
<td>K. Relakis</td>
</tr>
<tr>
<td>S. Sifakis</td>
</tr>
<tr>
<td>E. Vardaki</td>
</tr>
<tr>
<td>T. Vrekousis</td>
</tr>
<tr>
<td>I. Zouraraki</td>
</tr>
</tbody>
</table>

### Scientific Committee

<table>
<thead>
<tr>
<th>Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Makrigiannakis (Greece)</td>
</tr>
<tr>
<td>I. Messinis (Greece)</td>
</tr>
<tr>
<td>R. Ron-El (Israel)</td>
</tr>
<tr>
<td>A. Watrelot (France)</td>
</tr>
<tr>
<td>P. Drakakis (Greece)</td>
</tr>
<tr>
<td>S. Kalantaridou (Greece)</td>
</tr>
<tr>
<td>D. Loutradis (Greece)</td>
</tr>
</tbody>
</table>

### Invited Speakers / Chairmen

#### Foreign

- R. Campo (Belgium)
- M. Gergolet (Italy)
- S. Gerli (Italy)
- G. Grudzinskas (UK)
- P. Inaudi (Italy)
- U. Jeschke (Germany)
- A. Kavallaris (Greece/Germany)
- K. Khan (UK)
- L. Kiesel (Germany)
- A. Ljubic (Serbia)
- T. Motrenko (Montenegro)
- T. Roemer (Germany)
- L. Sabatini (UK)
- H. Sallam (Egypt)
- V. Tanos (Cyprus)
- A. Watrelot (France)

#### Greek

- G. Adonakis
- T. Agorastos
- I. Athanasaki
- G. Chrousos
- G. Creatsas
- K. Dafoopoulos
- N. Dalkalitsis
- E. Deligeorgiou
- P. Drakakis
- G. Farmakides
- M. Fraidakis
- P. Gasparis
- I. Giakoumakis
- A. Gravanis
- G. Grimpizis
- S. Kalantaridou
- L. Kientzeris
- S. Kolibianakis
- D. Kyrou
- D. Loutradis
- A. Makrigiannakis
- N. Maniadakis
- T. Mantzavinos
- A. Margioris
- M. Mastrominas
- I. Messinis
- S. Milingos
- G. Nikas
- T. Paraschos
- E. Paraskavaidis
- M. Paschopoulos
- G. Pistofidis
- K. Relakis
- A. Rodolakis
- B. Tarlatzis
- G. Tolis
- N. Vlachos
- K. Zikopoulos
Welcome Letter

Dear Colleagues and Friends,

It is a privilege for us to welcome you to the International Meeting of the Mediterranean Society for Reproductive Medicine (MSRM) in collaboration with the University of Crete. The Meeting is held in Crete, Greece from the 21st to the 23rd of October 2011 at the Gran Melia Hotel in Vathi, Agios Nikolaos, Crete.

This Meeting is interactive and allows young colleagues and experts to interact together. The theme of the Meeting is:

“Endometriosis
Current Management and Future Trends”

and its main topics are:

- Endometriosis: recent therapeutic approaches
- Pathogenesis of the disease - Diagnosis
- Adenomyosis
- Diagnostic dilemmas
- Clinical relevance and treatment options
- Surgical treatment
- Classical medical treatments
- New medical treatments
- Future trends
- Update on the pathobiology of endometriosis
- Endometriosis and art

We have no doubt that you will enjoy the Meeting that promises to be a rich and educational Scientific Program, taking place in the ideal setting of the island of Crete - an island with long history and culture, where the Minoan civilization flourished.

Wishing and hoping to share with you this scientific and cultural experience.

Professor Antonis Makrigiannakis, MD PhD
Meeting Chairman
Friday, 21 October, 2011

16.30-17.30 Session I

Chair: D. Loutradis, H. Sallam

- Role of brain hormonal microenvironment in neurodegeneration and neuroprotection
  - A. Gravanis, Greece
- Stress and Reproduction. A link with Endometriosis?
  - G. Chrousos, Greece

DISCUSSION

17.30-18.30 Session II

Chair: A. Margioris, I. Messinis

- The Enigma of Endometriosis is there a cure?
  - G. Grudzinskas, UK
- From Hippocrates to George N. Papanicolaou: A Medical Journey in time
  - G. Tolis, Greece

DISCUSSION

18.30-19.30 Session III: Pathogenesis of the disease - Diagnosis

Chair: G. Adonakis, L. Klentzeris, K. Dafopoulos

- Pathogenesis of endometriosis. Implantation or Metaplasia: What type of Disease
  - I. Athanasaki, Greece
- Immunology and Endometriosis: Is there a link?
  - U. Jeschke, Germany
- Endometriosis in Adolescence
  - E. Deligeoroglou, Greece
- Diagnosis of Endometriosis and Adenomyosis: Pitfalls of Current Methods
  - M. Paschopoulou, Greece

DISCUSSION

Saturday, 22 October, 2011

08.00-09.00 Oral Presentations I

Chair: I. Glakoumakis, M. Fraidakis

O.P.1 RUPTURE OF ENDOMETRIOMA IN A 14-YEAR OLD GIRL PRESENTING WITH ACUTE ABDOMINAL PAIN
  - Evangelinakis N.1, Koutoulakis I.1, Nikolaou M.1, Kotasos Th.1
  - 1Department of Obstetrics and Gynecology, General Hospital of Aghios Nikolaos

O.P.2 SPONTANEOUS UTERINE RUPTURE IN A PRIMIGRAVID WOMAN DUE TO ADENOMYSOSIS IN THE EARLY THIRD TRIMESTER
  - Nikolaou M.1, Kourea H.2, Antonopoulos K.2, Papadopoulos V.2, Adonakis G.2, Decavalas G.
  - 1Department of Obstetrics and Gynecology, General Hospital of Ag. Nikolaos, Crete
  - 2Department of Obstetrics and Gynecology, University Hospital of Patras, Rio, Greece

O.P.3 TRANSVAGINAL ULTRASOUND-GUIDED ASPIRATION OF OVARIAN ENDOMETRIOMAS
  - Nikolaou M.1, Zili P.1, Saltamavros A.D.2, Kardari M.1, Psachoulia C.1, Tsapanos V.1, Decavalas G.2, Adonakis G.1, Adonakis G.2
  - 1Department of Obstetrics and Gynecology, General Hospital of Aghios Nikolaos
  - 2Department of Cytology, University Hospital of Patras, Greece

O.P.4 ENDOMETRIOSIS IN A POSTMENOPAUSAL WOMAN WITHOUT HORMONE REPLACEMENT THERAPY
  - Department of Obstetrics & Gynecology of General Hospital of Chania, Kriti, Greece

09.00-10.30 Session III: Pathogenesis of the disease - Diagnosis

Chair: G. Adonakis, L. Klentzeris, K. Dafopoulos

- Pathogenesis of endometriosis. Implantation or Metaplasia: What type of Disease
  - I. Athanasaki, Greece
- Immunology and Endometriosis: Is there a link?
  - U. Jeschke, Germany
- Endometriosis in Adolescence
  - E. Deligeoroglou, Greece
- Diagnosis of Endometriosis and Adenomyosis: Pitfalls of Current Methods
  - M. Paschopoulou, Greece

DISCUSSION

10.30-11.00 COFFEE BREAK
<table>
<thead>
<tr>
<th>Time</th>
<th>Session / Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>11.00-12.00</td>
<td>Session IV: Receptivity / Implantation</td>
</tr>
<tr>
<td></td>
<td>Chair: I. Messinis, T. Mantzavinos</td>
</tr>
<tr>
<td></td>
<td>Morphological aspects of Endometriosis</td>
</tr>
<tr>
<td></td>
<td>G. Nikas, Greece</td>
</tr>
<tr>
<td></td>
<td>Endometrial Changes of Endometriosis</td>
</tr>
<tr>
<td></td>
<td>A. Makrigiannakis, Greece</td>
</tr>
<tr>
<td></td>
<td>DISCUSSION</td>
</tr>
<tr>
<td>12.00-13.30</td>
<td>Session V: IVF Specialists: Facing New Challenges... as Always!</td>
</tr>
<tr>
<td></td>
<td>MERCK SERONO SYMPOSIUM</td>
</tr>
<tr>
<td></td>
<td>Chair: D. Loutradis, V. Tarlatzis</td>
</tr>
<tr>
<td></td>
<td>Combination of recombinant gonadotropins:</td>
</tr>
<tr>
<td></td>
<td>Clinical experience shows the way ahead</td>
</tr>
<tr>
<td></td>
<td>N. Vlachos, Greece</td>
</tr>
<tr>
<td></td>
<td>Infertility treatment in the environment of</td>
</tr>
<tr>
<td></td>
<td>economic crisis: the value of pharmaco-economics</td>
</tr>
<tr>
<td></td>
<td>N. Maniadakis, Greece</td>
</tr>
<tr>
<td></td>
<td>Ovarian stimulation protocols: Individualization or “widely applied solutions”?</td>
</tr>
<tr>
<td></td>
<td>D. Kyrou, Greece</td>
</tr>
<tr>
<td></td>
<td>DISCUSSION</td>
</tr>
<tr>
<td>13.30-14.30</td>
<td>LUNCH</td>
</tr>
<tr>
<td>14.30-16.30</td>
<td>Session VI: Surgical Treatment</td>
</tr>
<tr>
<td></td>
<td>Chair: S. Milingos, G. Grimpizis, P. Parashos, P. Drakakis</td>
</tr>
<tr>
<td></td>
<td>What is good surgery for Endometriosis patients.</td>
</tr>
<tr>
<td></td>
<td>Cystectomy or Vaporization?</td>
</tr>
<tr>
<td></td>
<td>A. Watrelot, France</td>
</tr>
<tr>
<td></td>
<td>Laparoscopic management and complications of urinary deep infiltrating Endometriosis</td>
</tr>
<tr>
<td></td>
<td>G. Pistofidis, Greece</td>
</tr>
<tr>
<td></td>
<td>Laparoscopic nerve-sparing surgery of deep infiltrating endometriosis:</td>
</tr>
<tr>
<td></td>
<td>description of the technique and patients’ outcome</td>
</tr>
<tr>
<td></td>
<td>A. Kavallaris, Greece</td>
</tr>
<tr>
<td></td>
<td>Hysteroscopic management of Adenomyosis</td>
</tr>
<tr>
<td></td>
<td>R. Campo, Belgium</td>
</tr>
<tr>
<td></td>
<td>Endometriosis and Miscarriage: Is there any association?</td>
</tr>
<tr>
<td></td>
<td>M. Gergolet, Italy</td>
</tr>
<tr>
<td></td>
<td>DISCUSSION</td>
</tr>
<tr>
<td>16.30-17.00</td>
<td>COFFEE BREAK</td>
</tr>
<tr>
<td>17.00-17.30</td>
<td>Lecture</td>
</tr>
<tr>
<td></td>
<td>FARAN LECTURE</td>
</tr>
<tr>
<td></td>
<td>Chair: T. Mantzavinos, A. Makrigiannakis</td>
</tr>
<tr>
<td></td>
<td>Toward a modern concept of choice of gonadotropins in ART: the analysis of cost-effectiveness</td>
</tr>
<tr>
<td></td>
<td>S. Gerli, Italy</td>
</tr>
<tr>
<td>20.30</td>
<td>Opening Ceremony / Welcome Dinner</td>
</tr>
</tbody>
</table>
08.00-09.00 Oral Presentations II

**O.P.5**

OVEREXPRESSION OF CRH, UCN, CRHR1 AND CRHR2 IN ECTOPIC ENDOMETRIUM OF WOMEN WITH ENDOMETRIOSIS

Vergetaki A.1, Taliouri E.1, Neofytou E.1, Petsas G.1, Kardari I.1, Jeschke U.2, Friese K.2, Makrigiannakis A.1.

1Department of Obstetrics and Gynecology, Medical School, University of Crete, Greece
2Department of Obstetrics and Gynecology, Ludwig Maximilians University of Munich, Germany

**O.P.6**

THE EFFECT OF CRH ON GALECTIN-1 PATTERN IN ENDOMETRIOSIS AND GALECTIN-1 EXPRESSION IN ECTOPIC ENDOMETRIUM OF WOMEN WITH ENDOMETRIOSIS

Vergetaki A.1*, Jeschke U.2*, Taliouri E.1, Petsas G.1, Kardari I.1, Friese K.2, Makrigiannakis A.1.

1Human Reproduction Lab, Department of Obstetrics and Gynecology, University of Crete, Greece
2Department of Obstetrics and Gynecology, Ludwig Maximilians University of Munich, Germany.

* Equally contributed

**O.P.7**

POSSIBLE CORRELATION BETWEEN ENDOMETRIOSIS AND CERVICAL CANCER IMMUNE-MEDIATED MECHANISMS?

Taliouri E.1, Vergetaki A.1, Vrekoussis T.1, Petsas G.1, Neofytou E.1, Agorastos T.1, Makrigiannakis A.1.

1Laboratory of Human Reproduction, Dpt of Obstetrics & Gynecology, School of Medicine, University of Crete, Greece
24th Dpt of Obstetrics & Gynecology Clinics, School of Medicine, Aristotle University of Thessaloniki, Greece.

**O.P.8**

A CASE OF CONSERVATIVE MANAGEMENT OF PLACENTA INCRETA

Karamouti M.1, Tsetis D.2, Tzanakis M.3, Kondylis P.1, Relakis K.1, Rasidaki M.3, Chnakakis A.3, Karagiouzias T.1, Makrigiannakis A.1.

1IVF Unit – University Hospital of Heraklion, University of Crete
2Department of Radiology – University Hospital, University of Crete
3OB&GYN Department, General Hospital of Heraklion of Crete.

09.00-10.30 Session VIII: Classical Medical Treatments. Fertility Preservation

Chair: E. Paraskevaidis, T. Agorastos, K. Zikopoulos

Oral contraceptive pills for treatment of Endometriosis

P. Inaudi, Italy

Is there a need to treat Endometriosis Prior to IVF?

B. Tarlatzis, Greece

Fertility Preservation option in patients with severe endometriosis

S. Kolibiannakis, Greece

Ovarian hyperstimulation, Endometriosis and Ovarian Cancer

A. Rodolakis, Greece

DISCUSSION

10.30-11.00 COFFEE BREAK

11.00-12.00 Session IX: Innovation in the treatment of Endometriosis

**BAYER HELLAS SYMPOSIUM**

Chair: G. Creatsas, A. Makrigiannakis

Visanette® – a targeted approach to endometriosis treatment

L. Kiesel, Germany

Clinical experiences with Visanette® in endometriosis treatment

T. Roemer, Germany
<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
<th>Chair</th>
<th>Topics</th>
</tr>
</thead>
<tbody>
<tr>
<td>12.00-12.30</td>
<td>Lecture</td>
<td>M. Mastrominas, L. Sabatini</td>
<td>Does adenomyosis affect fertility? K. Khan, UK</td>
</tr>
<tr>
<td>12.30-13.30</td>
<td>Session X: Endometriosis &amp; Art</td>
<td>N. Dalkalitsis, G. Farmakides, S. Kalantaridou</td>
<td>Management of ovarian endometriotic masses prior to ART V. Tanos, Cyprus</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Ovarian Endometriosis anf, IVF-Is there a relationship? A. Ljubic, Serbia</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Obstetric morbidity in IVF - derived pregnancies in women with endometriosis H. Sallam, Egypt</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Outcome of IVF procedures in endometriosis T. Motrenko, Montenegro</td>
</tr>
<tr>
<td>13:30</td>
<td>CONCLUSIVE REMARKS</td>
<td>A. Makrigiannakis – P. Inaudi</td>
<td></td>
</tr>
</tbody>
</table>

DISCUSSION
Crete

Crete, the island of king Minos in the southern part of the Aegean Sea, is full of natural beauties to explore and enjoy. Picturesque ports and sandy beaches with transparent waters will help you relax and at the same time discover the continuing fascination and attraction of the island.

Venue

The Meeting is held in Agios Nikolaos, Crete at Gran Melia Hotel
Address: Vathi 72100, Crete, Greece, Tel.: +3028410-62600, Fax: +3028410-62622,
Web site: www.granmeliacrete.com

Dates

The Meeting is held from 21-23 October, 2011.

Key Dates

Deadline for reduced registration fees: August 31st, 2011
Full payment for Reservations: September 30th, 2011

Scientific Program

The Scientific program consists basically of State of the Art Presentations, Round Tables, Lectures, Case Studies, Oral Presentations

Continuing Medical Education

The MSRM International Meeting “Endometriosis-Current Management and Future Trends” has been accredited by the European Accreditation Council for Continuing Medical Education (EACCME-UEMS) with 12 CME-CPD credits.

Scientific presentations

The Meeting Hall will be equipped with slide projectors for single or double projections 50 x 50 mm slides (24 x 36 mm transparencies), overhead projector, Screen, Data display projector for Power Point presentation, laser pointers etc.

Slide and PC Reception

A slide and PC reception desk for acceptance and checking of slides and PC disks will be located nearby the Meeting Hall. All slides and PC disks should be clearly labeled with the author’s name and session’s name. Speakers are kindly requested to hand out their slides or their PC disks at least 2 hours prior to their respective presentation.

Certificate of Attendance

A certificate of attendance will be given to each registered participant, at the end of the Meeting.

Web site

The Meeting’s web site is: www.MediterraneanConferences.com

Secretariat and Travel Agency

For all inquiries regarding: Meeting Activities and functions, Registration, Letter of invitation, Accommodation and Travel Reservations, Technical Services, Exhibition, Sponsoring, please contact:
ERA Ltd., 17, Asklipiou Str., 106 80 Athens, Greece, Tel.: +30 210 3634 944
Fax: +30 210 3631690, e-mail: info@era.gr, Web site: www.era.gr.
Secretariat and Hospitality Desk
The Meeting Secretariat desk will be located nearby the Meeting Hall and will operate throughout the Meeting hours.

Language
ENGLISH is the official language of the Meeting. Simultaneous interpretation will be available.

Weather and dress
The weather in Crete during the month of October is sunny with very few windy days. The temperature ranges from 18° C to 25° C. For all outdoor evening events, sweater or jacket will be necessary.

Electric power
Electric current in Greece is 220 / 240 AC / 50 Hz. The plugs have 2 or 3 round pins similar to those in many European countries.

Liability and Insurance
The Organizers cannot be held responsible for any claim concerning liability, personal damage, lost, theft, illness, non-appearance of speakers etc. We recommend participants and exhibitors to cover these risks by a respective insurance. The Program is subject to change without notice. In case of cancellation of the event the registration fees will be refunded. No additional claims will be accepted.

Trade Exhibition
There is an exhibition of scientific products, pharmaceuticals, instruments, equipment and relevant materials at the Meeting Venue.

Registration Fees

<table>
<thead>
<tr>
<th>Description</th>
<th>Until August 31st, 2011</th>
<th>After September 1st, 2011</th>
</tr>
</thead>
<tbody>
<tr>
<td>General Participation</td>
<td>€ 300</td>
<td>€ 350</td>
</tr>
</tbody>
</table>

The registration fees for all Participants cover:
- Access to the Scientific Sessions and Exhibition
- Meeting material
- Welcome Reception
- Coffee breaks & light lunch

Accommodation Package

<table>
<thead>
<tr>
<th>Type</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>For All Participants</td>
<td>€ 270</td>
</tr>
<tr>
<td>Accompanying Person</td>
<td>€ 100</td>
</tr>
</tbody>
</table>

Rate includes: 2 nights accommodation bed & breakfast at the Gran Melia Hotel, in single room
Rate includes: 2 nights accommodation bed & breakfast at the Gran Melia Hotel, in double room with participant and the Welcome Dinner

Cancellation and Payment conditions are included in the Registration / Reservation Form.
Cancellation Conditions
Cancellation requests must be made to the Meeting Secretariat in writing.
- For cancellation of registration, received by August 26th, 2011, a refund of the total fee, less 25% as administration charge, will be made. After that date refunds for registration will not be possible.
- For cancellation of accommodation package, received by September 5th, 2011, a refund of the total fee, less 50% will be made.
- After that date refunds for accommodation package will not be possible.

Payment Conditions
- 50% of the accommodation package, payable to ERA Ltd, is required in order to confirm your Hotel Reservation
- Full payment for accommodation package should reach the Meeting Secretariat, not later than September 30th, 2011.

Method of Payment for Registration / Accommodation Package
Payment can be effected either:

a) By bank remittance stating the meeting’s title, as well as the name of the participant:
   - For Foreign Participants: To Bank of Cyprus - SYNTAGMATOS SQ. Branch - Mitropoleos 9, GR-105 57 - Athens, Greece, to the order of ERA Ltd Account No: 1 1 7 9 0 4 0
     (Swift Code: BCYPGRAA),
     IBAN Code: GR 690730001000000001179040
     Charges to be paid by sender
   - For Greek Participants: To Alpha Bank to the order of ERA Ltd Account No: 1 0 1.00.2002044307,
     IBAN Code: GR 660140 1010101002002044307
     Please enclose a copy of transfer receipt with the form.

b) By major credit cards.
Acknowledgements

The Organizing Committee of the MSRM International Meeting “Endometriosis – Current Management and Future Trends” Expresses its gratitude to the below Companies that generously contributed to its materialization:

Golden Sponsor

MerckSerono
Living science, transforming lives

MERCK

Bronze Sponsor

Bayer HealthCare

Sponsors

Biogène
Endoskopikí
Ferrin
LEO

ELPEN

Faran Laboratories s.a.

Ipsen

Leo

MSD

Novo Nordisk

Verishield
"ENDOMETRIOSIS
Current Management and Future Trends"

21 - 23 October 2011
Gran Melia, Vathi, Agios Nikolaos
Crete - Greece

Oral Presentations
O.P.1 RUPTURE OF ENDOMETRIOMA IN A 14-YEAR OLD GIRL PRESENTING WITH ACUTE ABDOMINAL PAIN
Evangelinakis N.,1 Koutoulakis I.,1 Nikolaou M.,1 Katasos Th.1
1Department of Obstetrics and Gynecology, General Hospital of Aghios Nikolaos

Aim: Present an unusual case of a teenager with a large ruptured endometrioma of the left ovary.

Case report: A 14-year-old girl presented at the emergency department of our hospital complaining for pain of the lower abdomen. Vital signs of the patient were within normal values. ER doctor palpated a mass and described a mild tenderness at the lower left quadrant of the abdomen. Transabdominal (no sexual intercourses) ultrasound revealed a 75x45mm cystic formation of the left ovary with clear margins and no diaphragms. Blood count showed Hct:39,8%, Hgb:13,4 and WBC: 14.900 (78,5% Neu). Patient was admitted in Ob/Gyn department and treated conservatively with antibiotic (clindamycin, due to allergy in cephalosporins and metronidazole). CT scan verified the findings of the U/S describing a 10 x 9x11cm cystic formation containing blood that does not infiltrate adjacent structures. No lymph nodes were detected. Within 24hrs, through which she was carefully monitored, Hct was 28%, Hgb: 9,16 and WBC: 11.700 (63% Neu). Due to the large size of the cyst patient underwent a laparotomy during which a ruptured endometriosic cyst of the left ovary was identified. No ovarian tissue could be identified at the circumference of the cyst and the cyst with the oviduct and any ovarian remnants were removed. Pathologic examination confirmed the diagnosis of endometrioma. Patient was released two days later with prescription for oral contraceptives.

Conclusion: Endometriosis is a relatively rare but possible diagnosis in teenagers and a transabdominal U/S should always be performed.

O.P.2 SPONTANEOUS UTERINE RUPTURE IN A PRIMIGRAVID WOMAN DUE TO ADENOMYOSIS IN THE EARLY THIRD TRIMESTER
Nikolaou M.,1 Kourea H.,2 Antonopoulos K.,2 Papadopoulos V.,2 Adonakis G.,2 Decavalas G.,3
1Department of Obstetrics and Gynecology, General Hospital of Ag. Nikolaos, Crete
2Department of Obstetrics and Gynecology, University Hospital of Patras, Rio, Greece
3Department of Pathology, University of Patras, Rio, Greece

Background: The spontaneous uterine rupture in primigravid woman is very rare obstetrical event with high rates of maternal and perinatal morbidity and mortality. Aim: To report a case of spontaneous rupture of an unscarred uterus due to adenomyosis in the third trimester.

Case Report: 33-year old primigravid woman was referred to our department because of severe acute abdominal pain and signs and symptoms of hemorrhagic shock. She had severe endometriosis and before 9 months underwent laparoscopic bilateral salpingectomy. Ultrasound examination performed at admission revealed a living, intrauterine fetus of 28 weeks gestational age with reduced amniotic fluid and presence of free peritoneal fluid. No vaginal bleeding observed and the cervix was closed on vaginal examination. The fetal heart rate was non-reassuring with decelerations and severe fetal bradycardia.
Emergency cesarean section revealed a massive hemoperitoneum and a complete uterine rupture in the fundus. A female infant weighting 1310 g was delivered. Subtotal peripartum hysterectomy with conservation of adnexae was performed. Histological examination revealed multiple foci of adenomyosis with decidual transformation at site of uterine rupture. The woman was treated with a full course of intravenous antibiotics and discharged home after 9 days postoperatively.

**Conclusions:** Spontaneous rupture of an unscarred uterus due to adenomyosis although is very rare should be considered in cases of uterine rupture. High-index of suspicion regardless of parity and early surgical intervention is the key to management of uterine rupture.

---

**O.P.3 TRANSVAGINAL ULTRASOUND-GUIDED ASPIRATION OF OVARIAN ENDOMETRIOMAS**

Nikolaou M.1, Zili P.1, Saltamavros A.D.2, Kardari M.3, Psachoulia C.3, Tsapanos V.2, Decavalas G.2, Adonakis G.2

1 Department of Obstetrics and Gynecology, General Hospital of Ag. Nikolaos, Crete.  
2 Department of Obstetrics and Gynecology, University Hospital of Patras, Greece  
3 Department of Cytology, University Hospital of Patras, Greece.

**Background:** An increased number of ovarian endometriomas in young women, are diagnosed during fertility investigation. We use the minimal invasive method of transvaginal ultrasound-guided aspiration for treatment of ovarian endometriomas due to simplicity, safety and efficacy on fertilization rate and overall pregnancy rate.

**Aim:** We report our experience with transvaginal ultrasound-guided aspiration of ovarian endometriomas.

**Methods:** This study took place in the Department of Gynecology and Obstetrics at the University Hospital of Patras, between January 2005 and June 2008. During this period 46 women were referred to our outpatient department after detection of a persistent ovarian cyst. Eight women (17.5%) had an ovarian endometriomas. After the detection of ovarian endometriomas, it was recommended to women to have gonadotropin-releasing hormone agonists (GnRH-agonist) injections monthly for 3 months. All statistics were performed using SPSS for windows, version 17.0.1 (Chigago, Illinois, USA).

**Results:** All aspiration procedures were successful with complete evacuation of cysts contents. Women with ovarian endometriomas have an increased incidence of recurrence of 62.5% in compared to others serous, serous-hemorrhagic cysts. The transvaginal ultrasound-guided aspiration of ovarian endometriomas appears to be a promising alternative treatment over surgery especially in cases where the surgical excision is technically difficult,, but its efficiency remains unclear due to the very high recurrence rates in a period of 6 months follow-up.

**Conclusions:** The issue of recurrences in ovarian endometriomas after transvaginal ultrasound- aspiration is still a present problem which made it difficult for the patients with symptoms or fertility treatments.
O.P.4 ENDOMETRIOSIS IN A POSTMENOPAUSAL WOMAN WITHOUT HORMONE REPLACEMENT THERAPY
Department of Obstetrics & Gynecology of General Hospital of Chania, Kriti, Greece

Background: Endometriosis is a benign, estrogen dependent, chronic gynecological disorder associated with pelvic pain and infertility during the reproductive age, although it can affect between 2 and 5% of postmenopausal patients, and generally occurs as a side-effect of hormone use.

Aim: The presentation of a case of endometriosis in a postmenopausal woman with no previous use of hormone replacement therapy (HRT) and no history of endometriosis or infertility.

Case Report: A 62-year-old woman (gravida 3, para 3) presented with acyclic pelvic pain. Pelvic ultrasound revealed a left ovarian homogeneous cystic mass approximately 5.5x4.8 cm in size. A Doppler blood flow study showed a resistive index of 0.53. The cancer antigen 125 (CA-125) serum level was measured as 16.7 U/ml. Alpha-fetoprotein and carcino-embryonic antigen levels were 7.3 U/ml and 6.2 U/ml, respectively. The patient’s menarche occurred at age 14 years and was followed by regular painless menses and menopause at age 52 years. She denied current or previous use of HRT. During bimanual examination, the patient complained of pain in the left adnexal topography. Laparotomy revealed a cystic left adnexal mass; no adhesions or other pelvic endometriotic lesions were observed. She was submitted to a total abdominal hysterectomy with bilateral salpingo-oophorectomy and subsequent histological analysis confirmed an ovarian endometriotic cyst.

Conclusion: In the treatment of postmenopausal women with suspect cystic adnexal mass, it is important in the differential diagnosis with malignancies, to be aware of endometriosis, even after the menopause.

O.P.5 OVEREXPRESSION OF CRH, UCN, CRHR1 AND CRHR2 IN ECTOPIC ENDOMETRIUM OF WOMEN WITH ENDOMETRIOSIS
Vergetaki A.1, Taliouri E.1, Neofytou E.1, Petsas G.1, Kardari I.1, Jeschke U.2, Friese K.2, Makrigiannakis A.1
1Department of Obstetrics and Gynecology, Medical School, University of Crete, Greece
2Department of Obstetrics and Gynecology, Ludwig Maximilians University of Munich, Germany.

Background: Endometriosis has been described as a benign, sex-hormone depended disease, characterised by the presence of ectopic endometrium-like tissue where several inflammatory factors are implicated. Its symptoms (mostly pain and infertility) are reported as constant stressors. Corticotropin releasing hormone(CRH), which is one of the main regulators of the HPA (hypothalamic-pituitary-adrenal) axis and urocortin (UCN) are neuropeptides, strongly related to stress and have been found to be expressed in eutopic and ectopic endometrium. They act through CRHR1 and CRHR2 receptors and they are implicated in several reproductive functions as inflammatory components.

Aim of the study: The aim of the study was to examine and compare the expression of CRH, UCN and their receptors CRHR1 and CRHR2 and their subtypes CRHR1β and CRHR2α in eutopic endometrium to that in ectopic endometrium of women with endometriosis.
**Materials and Methods**: Endometrial and endometriotic biopsy specimens were taken from women with endometriosis. The expression of CRH, UCN, CRHR1, CRHR2 and their subtypes CRHR1β, CRHR2α were tested via RT-PCR and immunostaining techniques. Cell line of endometrial cancer (Ishikawa cells) has been used, serving as endometriosis models.

**Results**: We confirmed CRH and UCN mRNA and protein expression in eutopic and ectopic endometrium of women with endometriosis and epithelial adenocarcinoma cell line. We showed that CRHR1β and CRHR2α are expressed in ectopic endometrium of women with endometriosis at mRNA and CRHR1 and CRHR2 at protein level, as we have firstly tested their mRNA expression in Ishikawa cell line, resembling endometriosis. Comparing CRH, UCN, CRHR1β and CRHR2α mRNA expression in both eutopic and ectopic endometrium of the same women with endometriosis, their expression was found to be significantly higher (P<0.05) in ectopic endometrium to that of eutopic endometrium of the same women with endometriosis.

**Conclusion**: These results showed for the first time that CRH and UCN receptor subtypes CRHR1β and CRHR2α are expressed in endometriotic sites and that CRH, UCN and their receptors are more strongly expressed in ectopic rather than eutopic endometrium in women with endometriosis at mRNA level. These new data reveals new possible immunoregulatory roles of CRH and UCN in endometriotic sites and enforces the modulatory role of these molecules in reproductive functions.

**Key words**: endometriosis, endometrium, CRH, UCN, CRHR1β, CRHR2α, implantation

---

**O.P.6 THE EFFECT OF CRH ON GALECTIN-1 PATTERN IN ENDOMETRIOSIS AND GALECTIN-1 EXPRESSION IN ECTOPIC ENDOMETRIUM OF WOMEN WITH ENDOMETRIOSIS**

Vergetaki A.¹*, Jeschke U.²*, Taliouri E.¹, Petsas G.¹, Kardari I.¹, Friese K.², Makrigiannakis A.¹

¹Human Reproduction Lab, Department of Obstetrics and Gynecology, University of Crete, Greece

²Department of Obstetrics and Gynecology, Ludwig Maximilians University of Munich, Germany.

* Equally contributed

**Background**: Galectins are carbohydrate-binding proteins, found on the cell surface and play an important role in cell adhesion, signalling and survival. Galectins have a pro- or anti-inflammatory role and a modulating role on T cells, so that may affect immunological mechanisms. Endometriosis is a sex hormone dependent and inflammatory disease, where endocrine / paracrine influences and immunological aspects are involved. The main symptoms (pain and infertility) of this disease are considered as stressors, so the neurohormone CRH (corticotrophin releasing-hormone) has been detected at endometriosis sites and is increased comparing to eutopic endometrium. Galectin-1 has been found to be expressed in human endometrium and decidua apart from other tissues.

**Aim of study**: The aim of this study was to elucidate the effect of CRH on the galectin-1 pattern in endometriotic lesions and to compare the expression of galectin-1 in healthy women’s eutopic endometrium to the expression of this galectin in ectopic endometrium of women with endometriosis.

**Materials and Methods**: Hec1B and Ishikawa cells were used serving as endometriosis models in order to clarify the effect of CRH in galectin-1 expression at endometriotrionic
sites. Endometrial biopsy specimens from women without endometriosis and from ectopic endometrium from women with endometriosis were used for galectin-1 detection.

**Results:** By immunocytochemistry, this study revealed that CRH downregulates the galectin-1 expression in Ishikawa and Hec 1B cell lines in a dose dependent manner after a 72h stimulation. Moreover, this study has shown that galectin-1 is decreased in endometriosis sites (IRS:2.45) compared to that in healthy eutopic endometrium (IRS:10.27) using immunohistochemistry and is detected in stromal cells.

**Conclusion:** The fact that CRH downregulates galectin-1 expression in ectopic endometrium combined with the fact that galectin-1 expression is downregulated in endometriotic tissue and that galectin-1 stimulates apoptosis of activated T cells, we could think of T cell survival in endometriotic sites. Furthermore, this strengthens CRH and galectin-1 role and contribution to reproductive function problems that women with endometriosis are exposed.

**Key words:** galectin-1, endometrium, endometriosis, CRH

---

**O.P.7 POSSIBLE CORRELATION BETWEEN ENDOMETRIOSIS AND CERVICAL CANCER IMMUNE-MEDIATED MECHANISMS?**

Taliouri E.1, Vergetaki A.1, Vrekoussis T.1, Petsas G.1, Neofytou E.1, Agorastos T.2, Makrigiannakis A.1

1Laboratory of Human Reproduction, Dpt of Obstetrics & Gynecology, School of Medicine, University of Crete, Greece.

24th Dpt of Obstetrics & Gynecology Clinics, School of Medicine, Aristotle University of Thessaloniki, Greece.

**Background:** Cytokines, such as Human beta defensins (hBDs), are natural anti-microbial peptides, having a central role in the initiation-propagation-regulation of Immune-Inflammatory responses (I/I). They act as innate-immune system-key mediators, trying to prevent infections, expressed at epithelial surfaces throughout the female genital tract (1-3).

Corticotropin Releasing Hormone (CRH) is as well expressed during an I/I process, acts as autocoids and indirectly in an anti-inflammatory fashion, enhancing resistance to inflammatory response (2).

Endometriosis, is a polygenically inflammatory disease with multifactorial biopathogenesis (3), which development may depend on cell-mediated immunity changes. Secreted pro-inflammatory cytokines; hBD1-4 and CRH could potentially contribute to pathogenesis, early establishment, progression and pathophysiology of the disease (2-3). Data suggest an increased risk of ovarian cancers, in women with endometriosis.

Cervical cancer is an inflammatory process caused by HumanPapillomaVirus infection. A complex chemokine-cytokine network, influence the extent and phenotype of immune-cells infiltration, tumour cell growth, survival and migration. Cytokines have profound effects on establishment and further progression of those diseases.

**Aim:** Causative relationship of pro-inflammatory cytokines (hBD-CRH) secretion pattern between endometriosis and cervical cancer development. Potential use as disease biomarkers.

**Materials & Methods:** Immunohistochemistry staining was conducted to estimate hBD1-Hbd2-CRH expression to human squamous cervical carcinoma tissues.
HeLa cell line was used. hBD1-Hbd2-CRH intracellular localization was investigated by indirect immunofluorescence. CRH presented was assessed with RT-PCR.

**Results:** hBD1-Hbd2-CRH protein expression was identified in human cervical cancer and detected in the cytoplasm of Hela cells. CRH mRNA was further identified in HeLa cells.

**Conclusion:** hBD1-Hbd2-CRH expression has been established in human cervical cancer development. A similar pattern of expression has been reported during endometriosis (3). These findings may have indicated the similarities of immune defense repertoire in response to infection at sites, throughout the female reproductive tract.

**References**


---

**O.P.8 A CASE OF CONSERVATIVE MANAGEMENT OF PLACENTA INCRETA**

Karamouti M.1, Tsetis D.2, Tzanakis M.3, Kondylis P.1, Relakis K.1, Rasidaki M.3, Chnarakis A.3, Karagkiouzis T.1, Karantanas A.2, Makrigiannakis A.1

1IVF Unit – University Hospital of Heraklion, University of Crete
2Department of Radiology – University Hospital, University of Crete
3OB&GYN Department, General Hospital of Heraklion of Crete

**Background:** Placenta implantation disorders are counted among the leading causes of emergent hysterectomy in young reproductive women.

**Aim:** To present a case of conservative treatment of placenta increta, diagnosed following spontaneous premature labor, in a primigravida women.

**Case Report:** A 27 year old primigravida, with free previous obstetric and medical history, had a spontaneous pregnancy, which was complicated with 3 episodes of vaginal bleeding and premature contractions, between 20-25 weeks of gestation, managed with tocolysis and hospitalization. At 25 weeks of pregnancy the patient had a premature, breech labor of an alive, ablebodied, male newborn, weigthening 620gr. Spontaneous placenta delivery did not follow and a digital separation effort was made in the operating theatre, but was unsuccessful, since the placenta was firmly attached to the myometrium. Patient was not bleeding at the time and was hemodynamicaly stable and was managed with oxytocin and antibiotics and was further investigated with ultrasound (U/S) and magnetic resonance imaging (MRI). Based on U/S, MRI and the pathology report, the diagnosis of placenta increta was set. Since the patient wished to save her uterus, a conservative management was chosen, with methotrexate, which reduced only partially the vascularization and the mass of the retained placenta. Arterial embolization of the mass followed, which totally abolished placenta vascularization, preserving the normal vascularization of the uterine wall. Retained placenta was spontaneous expelled, with no complications.

**Conclusions/Summary:** Although hysterectomy remains the gold standard in the management of placenta increta, alternative, conservative management options need to be offered especially when future fertility is wished.
SESSION I

Role of brain hormonal microenvironment in neurodegeneration and neuroprotection

A. Gravanis
Dept. of Pharmacology, School of Medicine, University of Crete, Foundation of Research & Technology-Hellas IESL-FORTH, Heraklion GR

Neurosteroids, produced by neurons and glia, have been shown to exert strong neuroprotective and neurogenic properties, while their decline during ageing is associated to neurodegenerative diseases. We have shown that endogenous neurosteroid dehydroepiandrosterone (DHEA), protects neuronal cells against apoptosis at nanomolar concentrations (Charalampopoulos et al, PNAS 2004), via binding to specific plasma membrane receptors (Charalampopoulos et al, FASEB J 2006), rapid activation of prosurvival kinases MEK1/2/ERK1/2, and PI3K/Akt, the induction of transcription factors CREB and NFKB and the transcriptional activation of anti-apoptotic Bcl-2 genes. Recently, we have described the nature of DHEA membrane binding sites, which in fact are the receptors of the main neurotrophin, nerve growth factor (NGF) (Lazaridis et al, PLoS Biol 2011). Indeed, DHEA exerts its neurotrophic effects by directly interacting with TrkA and p75NTR receptors of NGF, efficiently inducing TrkA phosphorylation, and NGF receptor-mediated signaling; Shc, Akt, and ERK1/2 kinases down-stream to TrkA receptors and TRAF6, RIP2 and RhoGDI interactors of p75NTR receptors, preventing the apoptotic loss of NGF receptor positive sensory and sympathetic neurons in ngf−/− null mice. These findings may have important pharmacological applications in the treatment of neurodegenerative diseases. DHEA cannot be given long term, due to its in vivo conversion to estrogens and androgens. On the other hand, polypeptidic NGF does not cross the brain blood barrier (BBB). We have recently synthesized 17 spiro-analogs of DHEA with strong neuroprotective effects and deprived of estrogenic or androgenic actions (Calogeropoulou et al, J Med Chem 2009). These synthetic neurosteroids cross the BBB, interact with NGF receptors and mimic various actions of NGF. They are now tested as potential therapeutic agents in various animal models of neurodegenerative diseases.

SESSION II

The enigma of endometriosis: is there a cure?

Gedis Grudzinskas
London, UK

Since by virtue of the definition of enigma, endometriosis is a puzzling or inexplicable occurrence or situation, it is not surprising that a cure does not exist for this condition. This being the case, we are left to address not the condition but the patient and her symptoms, clinicians needing to call on all their skills to balance the patient requirement for “cure”, with the consequences of the intervention in relation to the woman’s fertility, sexuality and general well being. Cure in this context is limited to restore and preserve health and wellbeing. How well the medical and scientific community has achieved this is reflected by the number of self-help organisations, scientific meetings and journals dedicated to this subject alone. A Google enquiry at the time of writing revealed: endometriosis=11 million hits; adenomyosis=568,000; fibroids=3.5 million hits. Theories on the aetiology of endometriosis include implantation; metaplasia; genetic and more recently environmental. A novel approach developed by Australian researchers led by Ian Fraser “proposes that women who develop endometriosis are shedding endometrial stem cells from basal endometrium during menstruation. These rare cells (only present in very small numbers in the en-
Endometriosis is classically defined as the outgrowth of endometrial glands and stroma at extrauterine sites often associated with infertility, dysmenorrhea and chronic pelvic pain. The most common ectopic implants are located in the ovaries, fallopian tubes, vagina, cervix, uterosacral ligaments or in the rectovaginal septum while unusual implantation sites include laparotomy scars, pleura, lung, diaphragm, kidney, spleen, gallbladder, nasal mucosa, spinal canal, stomach or even breast.

Pathogenesis of Endometriosis

Although endometriosis establishment and progression is yet not clear, it is generally accepted that the disease arises from the implantation and growth of ectopic endometrial tissue into the peritoneal cavity following retrograde menstruation [1]. On the other hand, the lymphatic transport the-
ory, proposes that endometriosis first develops as metastatic foci of uterine tissue transported to other organs by way of the lymphatic system or the bloodstream [2]. Such hypothesis could explain the distal endometriotic implants. The pluripotent cell theory proposed in 1898 by Iwanoff, suggests that the pluripotent cells within the peritoneal mesothelium, which are present in the endometrium since the embryonic life of a female, upon stimulation by the retrograde menstruation are transformed into active endometrium [3], whereas Batt and Smith in 1989 suggested that the ectopic placement of endometrial cells occurs during the fetal life of a female embryo, where the cells that are programmed to form the endometrium stay outside the uterine wall and therefore endometrial cells are placed at a wrong position before woman’s birth [4]. Metaplasia can be considered as another cause for endometriosis development, where transformation of coelomic epithelium into endometrial-type glands in response to as yet unknown stimuli, could explain endometriosis in unusual sites. Coelomic metaplasia is also believed to explain the occurrence of endometriosis in women who have undergone total hysterectomy and are not taking estrogen replacement [5]. Further candidate hypotheses for the development of endometriosis are chemicals, candida infection or abnormalities, while various observations show that endometriosis is a genetic and pre-determined disease. Immune alterations, including increased number and activation of peritoneal macrophages, decreased T-cell cytotoxicity, increased circulating antibodies, as well as cytokines and growth factors in the environment of the abdominal cavity are also thought to contribute to the development and progression of endometriosis.

**Endometriosis as a disease**

Whatever the establishment mechanism, the implanted tissue expresses steroid receptors similar to normal endometrium and follows the hormonal menstrual cycle. Thus, every month endometriomas fill with blood, thicken, break down and bleed. In the absence of a natural root for the blood to exit, the implants develop into endometriotic cysts, spots or patches, which may grow and reseed as the menstrual cycle continues. Internal bleeding leads to the development of an inflammatory response, neovascularization and fibrosis, which is responsible for the clinical consequences of this disease. An important mechanical cause for infertility includes the limited elasticity of organs, which diminishes the possibility of ovum uptake by the fallopian tubes. An additional and perhaps more important parameter to infertility and pathogenicity is the cytokine imbalance induced by endometriomas.

Since endometriomas do not grow in the privileged site of uterus, they trigger systemic mechanisms to the female organism leading to significant changes of the cytokinetic profile. Thus, interleukin-1β and the vascular endothelial growth factor increase in the serum of endometriotic women possibly to facilitate angiogenesis [6]. Inteleukin-6 also increases in cases of endometriosis ensuring proliferation of endometrial cells, stimulates decidualization but becomes toxic to the late embryo [6]. The increased levels of interleukin-8 attract neutrophils to the endometriotic sites and facilitate angiogenesis [6]. By the same token, interleukin-10 and colony stimulating factor-1 increase in the serum of endometriotic women probably due to high numbers of activated macrophages in the endometrium [6, 7]. Granulocyte-macrophage colony stimulating factor is also found to increase in endometriosis, especially during the secretory phase of the menstrual cycle [6]. The increased levels of tumor necrosis factor-α during endometriosis ensure agglutination of endometrial cells to the epithelium [6]. Similarly, interferon-γ (IFN-γ) is also found increased in the serum and peritoneal fluid of endometriotic women [6]. Interleukin-15 is known to induce production of IFN-γ and increases in the peritoneal fluid of endometriotic women as well [8].

In addition to cytokines, another family of immune molecules found to be disturbed during endometriosis includes soluble HLA molecules. The levels of soluble class-I and class-II HLA proteins are found to significantly decrease in the serum of women suffering from endometriosis [9]. Yet, there is no information on whether and how these molecules can affect the early gestational stages.

Finally another important parameter that has to be considered is the heterogeneity of endometriomas as to oestrogen and progesterone receptor levels, the level of vascularization (CD34 expression) and the amount of nerve fibers (S100 expression) [10], which may dictate differential development and the need of different pharmaceutical behavior. Indeed, the human endometrial Ishikawa cells, which express estrogen (ER) and progesterone (PR) receptors and the MFE-319 cell line that express PR but not express ER receptors [11], both represent human endometrium ade-
nocarcinomas and display differential ability to implant. Thus, when Ishikawa or MFE-319 cells were administered to estrus circle synchronized young mice only Ishikawa cell inoculation showed intense signs of neovascularization, edema and implantation of cells [12]. It seems that endometriosis should no more be considered as a uniform pathologic condition. Characterization of the endometrioma could probably dictate specific therapeutic approach for each patient.


Immunology and Endometriosis: Is there a link?
Expression of galectins, cytokines and enrichment of dendritic cells in the ectopic endometrium of women with endometriosis and in vitro stress effects

Udo Jeschke a, Elisabeth Geitner, Christina Kuhn, Klaus Friese a and Antonis Makrigiannakis a
aDepartment of Obstetrics and Gynecology, Ludwig-Maximilians-University, Munich, Germany
bDepartment of Obstetrics and Gynaecology, Medical School, University of Crete, Iraklion, Greece

BACKGROUND: Galectins are carbohydrate-binding proteins and can be found on the cell surface. The aim of our study was to compare the expression of galectin 1 and galectin 3 in healthy women’s ectopic endometrium to the expression of these galectins in the ectopic endometrium of women suffering from endometriosis. The neurohormone CRH (Corticotropin releasing hormone) has been detected in increased levels in endometriosis sites. We investigated the effect of present CRH on the galectin 1/3 expression in endometrium cells in vitro.

MATERIALS AND METHODS: Endometrial biopsy specimens were taken from the endometrium of women without endometriosis (n=15; controls) and from ectopic endometrium tissue (ovarian and pelvic endometriotic implants) of endometriosis patients (n=54). Expression of galectin 1/3, IL-15 and DC-Sign were detected using the ABC-staining-method and IRS-scoring for comparison of staining results. In addition, two different lines of endometrium cancer cells served as a model for endometrium cells: Hec1B and Ishikawa cells. Both cell lines were incubated in vitro for 72 hours with different concentrations of CRH (0, 1, 10, 100 and 1000 ng/ml). The cells were fixed and we evaluated their galectin expression using the similar staining and analysing methods as described above.

RESULTS: We could show that galectin 1/3 expression in endometriosis tissue was decreased compared to the control samples of healthy endometrium. Within healthy endometrium as well as in endometriosis lesions galectin 1 has been detected nearly exclusively in stromal cells whereas galectin 3 has been found mainly in glandular cells. In addition, we identified a significant upregulation of DC-Sign in ovaries with endometriosis lesions. These ovaries showed also strong expression of IL-15. With cell culture and immunohistochemical staining we demonstrated that the presence of increased levels of CRH lead to a clearly reduced galectin 1 expression in model cell lines.

CONCLUSION: Results of this study showed a downregulation of galectin 1 in endometriosis lesions. Galectin 1 stimulates apoptosis of activated T cells. Therefore its diminished expression...
in endometriosis could be responsible for a decreased induction of lymphocytic apoptosis, in other words for an augmented T cell survival. In other studies increased levels of T-cells have been found in the eutopic and ectopic endometrium of women with endometriosis and especially within stromal cells of their ectopic endometrium. In addition, higher numbers of dendritic cells were found in ovaries with endometriosis and IL-15 seems to be involved in the upregulation of the immune cascade, which seems to be triggered by stress.

Endometriosis in Adolescence

Efthimios Deligeoroglou, Nikolaos Athanasopoulos, George Creatsas
Division of Pediatric – Adolescent Gynecology and Reconstructive Surgery
2nd Department of Obstetrics and Gynecology, University of Athens, Medical School, “Aretaieion” Hospital, Athens, Greece.

INTRODUCTION
Endometriosis has long been recognized as a condition affecting mainly reproductive-age women, but studies reveal that endometriosis rates in adolescent patients undergoing diagnostic laparoscopy for secondary dysmenorrhea and chronic pelvic pain evaluation, ranges from 19% to 75%. Moreover, it should be noted that 66% of adult patients report onset of pelvic pain symptoms even earlier from the age of twenty. Endometriosis has also been associated with the existence of uterovaginal anomalies, such as complete transverse vaginal septum, imperforate hymen and cervical agenesis, which in the majority of the cases, are diagnosed in adolescence.

CLINICAL PRESENTATION AND EVALUATION OF THE PATIENT
In adolescence the main symptom that leads the patients to seek for medical advice is pelvic pain. In most cases (62.6%), pain is both cyclic and acyclic, while more rarely endometriosis presents with acyclic or cyclic pain alone. Dyspareunia, gastrointestinal or urinary symptoms, menstrual disorders and vaginal discharge are other symptoms often reported by the patients. Severity of the symptoms is proportional to the progression of the disease. Initial investigation of the patient should include a thorough medical history and a careful clinical examination. Specific questions should be made regarding the frequency and the duration of the pain, as well as its association with bowel, bladder or sexual function.

The definitive diagnosis can only be set through laparoscopy and biopsy. The criteria proposed by the American Society for Reproductive Medicine (ASRM) should be used for the staging of the disease. Unlike adult patients who, in most of the cases, have the classic black/grey “powder burn” endometriotic implants, adolescents have stage I (77-92%) or stage II (8-22%) disease with red, white or clear lesions. Patients with endometriosis due to outflow obstruction tend to have more extended disease, but remittance is established as soon as the anatomic defect is surgically corrected.

TREATMENT OF ENDOMETRIOSIS IN ADOLESCENCE
Treatment of adolescents with endometriosis should focus to the relief from the symptoms, to the suppression of the disease, as well as to the preservation of future fertility, while it should always be individualized according to patient’s age, stage of the disease and severity of the symptoms. Treatment options include:
Non-steroidal anti-inflammatory drugs (NSAIDs): As early stage endometriotic lesions, which are commonly seen in adolescence, are documented to actively produce prostaglandins, NSAIDs can be used for the treatment of dysmenorrhea in these patients.

Oral Contraceptive Pills (OCPs): Administration of OCPs is considered to be the first line treatment for endometriosis in adolescence. OCPs have a very low adverse effect profile, and can be taken safely for a long time period. They act by suppressing the hypothalamic-pituitary-ovarian axis, inducing a hypoestrogenic environment, which inhibits endometriotic implant growth, and ovulation, which alleviates from luteal-phase symptoms of endometriosis. Continuous use of OCPs is suggested, despite the possibility of breakthrough bleeding.

GnRH agonists: GnRH agonists (GnRHa) cause a reversible suppression of the hypothalamic-pituitary axis, thus inducing a hypoestrogenic state, thus controlling growth and bleeding of endometriotic implants. Treatment with GnRHa has been associated with adverse effects on patients’ peak Bone Mass Density (BMD) accumulation. It is suggested that GnRHa should not be offered as a first line of treatment in adolescents younger than 16 years old. Moreover the U.S. Food and Drug Administration (FDA) has not approved prescription for course of therapy lasting longer than six consecutive months. Add-back therapy with norethindrone acetate or with combination of estrogens combined with medroxyprogesterone acetate, can help reducing the adverse effects associated with the administration of GnRHa and minimize bone density loss.

Depot Medroxyprogesterone Acetate (DMPA): Progestogen-only therapy acts by suppressing gonadotropins and causing decidualisation, necrosis and absorption of functional endometrial implants. DMPA provides effective relief from endometriosis symptoms, but there are concerns towards use in adolescence due to its negative effect on bone mineralization.

Danazol: Danazol acts by creating a hypoestrogenic environment (and consequently inducing endometrial atrophy) while also raising androgen levels. Although it has been a very popular therapeutic option during the 1980’s, its adverse effects (weight gain, bloating, decreased breast size, acne, oily skin and hirsutism), make it an unpopular therapeutic option for adolescents.

Surgical treatment: Surgical excision has also been proved to be effective treatment for pain in patients with endometriosis. The need for fertility preservation makes radical procedures like oophorectomy and hysterectomy inappropriate in adolescence, even in patients with severe endometriosis. The surgeon must be familiar with the appearance of early stage endometriotic lesions that are commonly found in adolescents. Postoperative hormonal treatment is imperative in order to reduce the possibilities of a recurrence.

CONCLUSIONS
Endometriosis is a condition affecting both adult women and adolescents, but there are significant differences in the characteristics of the disease between these groups. Adolescents usually present in a less advanced stage with early atypical lesions, while young women tend to have classic “powder burn” lesions and a more advanced stage of the disease. Treatment also differs between these two groups, as the necessity of fertility preservation and the immaturity of the skeletal system, dictates the use of different therapeutic schemes.

Diagnosis of Endometriosis and Adenomyosis: Pitfalls of Current Methods

M. Paschopoulos
Associate Professor of Obstetrics and Gynecology, Medical School of the University of Ioannina Greece

Endometriosis and adenomyosis are two common, non-neoplastic gynecological disorders, mainly affecting premenopausal women. They are defined by the presence of endometrial tissue (stroma and glands) in ectopic sites. In endometriosis, these sites are detected outside the uterus¹. In adenomyosis, they are found inside the myometrial layer of the uterus, with surrounding smooth muscle hyperplasia².

At present, there is no simple, reliable, non invasive diagnosis for neither one of them; their pres-
ence is presumed on the basis of clinical symptomatology, therefore their prevalence can not be estimated accurately. However, endometriosis is thought to be present in 10-15% of women of reproductive age, whilst adenomyosis is found in a median 40% of hysterectomy specimens (the frequency varies from 5% to 70%, if a rigorous microscopic analysis is performed), with concomitant endometriosis being present in an estimated 10-15% of cases. Histology is needed for a definitive conclusion regarding the presence or absence of endometriosis and adenomyosis, so there is usually an unavoidable delay from the onset of clinical symptomatology to the diagnosis. In the case of endometriosis, this delay could be as long as 7 to 10 years, depending on the level of provided care, number of symptoms and Body Mass Index. Unfortunately, the delay may be even longer in young age patients and in severe cases. This highlights the need for a continuous assessment of the diagnostic tools and methods available, so as to ensure their optimal use, and to help avoid potential diagnostic pitfalls.

Current methods for the diagnosis of endometriosis, and their potential pitfalls
Although a complete history and physical examination, including speculum and bimanual palpation, will probably be of help to the physician, there is no pathognomonic characteristic that will actually place the diagnosis of endometriosis beyond any doubt; however, both history and clinical assessment could suggest the benefits of imaging, prior to surgery. The misdiagnosis of a syndrome resembling endometriosis (eg IBS, or IC/PBS) should not escape the physician’s differential diagnosis. At present, laparoscopy is the golden standard for the diagnosis or exclusion of endometriosis. Unfortunately, the optical detection of endometriosis-like lesions does not seem to be enough to establish the diagnosis; it has been shown that a high percentage of these “optically diagnosed” cases is misdiagnosed as endometriosis, yet it is not. Therefore, the ideal approach is to have a histological specimen from the lesion under investigation.

Sonography, especially transvaginal, is the imaging modality mostly used for the detection of endometriosis-associated lesions in the female pelvis, the bowel, the bladder, the vagina, and the rectovaginal septum. In the hands of an experienced sonographer, it could also be used for the clinical assessment of pelvis and vagina in cases of deep infiltrating endometriosis (DIE). The use of transvaginal sonography has been found to increase its sensitivity and negative prognostic value when using ovarian mobility, site-specific tenderness, and peritoneal pseudocysts as soft markers. Magnetic Resonance is much more expensive than sonography, but it seems to be superior in guiding surgical approaches for patients with suspected endometriosis, especially in cases of DIE, or bowel and bladder lesions. As for double contrast barium enema (DCBE), it could be helpful in discerning bowel wall involvement; in this case, the experience of the radiologist is of utmost importance. The main pitfall is to misinterpret the findings or else DCBE should be used before MRI in cases of suspected orthosigmoid lesions, due to its lower cost.

A continuous research is being held for the identification of those plasma proteins that could be used as markers for a safe, and cheap non invasive diagnosis of endometriosis. CA-125, CA 19-9, IL-6, IL-8, hs CRP, TNF-a are a few of the proteins that have been tested alone or in groups in various studies. Although some of the results seem promising, there is still no robust evidence that a marker shows high sensitivity and specificity, so as to allow the use of a new test on the market.

Current Methods for the diagnosis of adenomyosis, and their potential pitfalls
Just as in endometriosis, the clinical diagnosis of adenomyosis is not easy because there are no pathognomonic symptoms and signs. It is difficult to conclude that uterus is enlarged due to adenomyosis and not because of leiomyomata. Even when using transvaginal sonography, it is not easy to detect the adenomyotic lesions, especially if they are focal (new treatments). Nevertheless, transvaginal sonography in the hands of experienced operators could provide enough evidence about the diagnosis, such as the following: asymmetrical thickening of the posterior and anterior walls, hypechoic areas scattered through the myometrium, heterogenous myometrial echotexture, and linear striations radiating out from the endometrium. It could be difficult to identify the above-mentioned features, in cases of fibroid uteri. In these cases, MRI could be of significant help. Also, this modality could be useful in delineating the location and extent of the lesion and in monitoring the evolution of the disease in patients re-
ceiving hormonal therapy\textsuperscript{14}. However, it is easy to make the wrong diagnosis in a series of cases, eg during menstruation, or during myometrial contractions. Also, it is easy to miss the diagnosis when an adenomyoma or an adenomyotic cyst is present. As for hysteroscopy, it is obvious that it provides good quality of data to support the diagnosis of adenomyosis, although obtaining adequate hysteroscopy-guided biopsies is not at all an easy task. During the procedure, it is important to remember that the differential diagnosis of adenomyosis includes malignant tumors of the uterine corpus\textsuperscript{15}.

Future Perspectives
The optimal modality for the diagnosis of endometriosis and adenomyosis is still an unsolved mystery. The support of new ideas in the field is of extreme importance, so as to help it to be solved. In this context, there is an ongoing experimental study using real time hyperspectral imaging during the hysteroscopic depiction of the various anatomic structures, which will be used during laparoscopy too. The preliminary results of this study are most promising.

REFERENCES
Endometrial Changes of Endometriosis

Professor Antonis Makrigiannakis, MD, PhD
Department of Obstetrics and Gynecology, Medical School, University of Crete, Greece

Endometriosis is a benign estrogen-dependent chronic disease affecting the 10% of women of reproductive age. It is characterised by the presence of endometrial-like tissue, including stroma and epithelium, in multiple sites outside the uterine cavity. The most common clinical symptoms of this chronic condition are pelvic pain and infertility. There are several theories concerning its pathogenesis which still remain to be elucidated. As endometriosis is not only a sex hormone dependent but inflammatory disease as well, endocrine/paracrine influences, immunological aspects and the function of eutopic endometrium are involved. As a result, the expression of growth factors, cytokines, several immune cells and hormones in eutopic and ectopic endometrium, are implicated in infertility profile of endometriosis patients. Ectopic and eutopic endometrium are histologically similar but have biochemical differences. A very interesting approach of this disease is the differences between the eutopic endometrium of women with and without endometriosis. Eutopic endometrium of women with endometriosis shows crucial changes in structure, proliferation, apoptosis, immunity, adhesion molecules, steroid, cytokine, gene and protein production, but there is also a controversy concerning the data that is available for these aspects. The alterations of eutopic endometrium of women with endometriosis are of great importance as they can possibly explain the pathogenesis and infertility profile of endometriotic women, taking into account that endometrial decidualization and embryo implantation are the fundamental processes leading to an effective pregnancy.

Key words: endometrium, endometriosis

Combination of Recombinant Gonadotropins:
Clinical Experience shows the way ahead

N. Vlachos

33 years since Louise Brown’s birth, our remarkable clinical experience and the clinical trials’ results have shown that, in the vast majority of the patients, FSH monotherapy is adequate for the ovarian stimulation in the frame of IVF/ICSI cycles. Meanwhile, there is strong evidence that in particular subpopulations the co-administration of LH may have a positive influence so as to be a reliable alternative treatment.

Recent bibliography has been specially focusing on two groups of patients:
• women of advanced reproductive age and
• poor responders

There is quite interesting data supporting the conclusion that infertile patients with the above characteristics may benefit by the administration of 75-150 IU rec-LH and get improved final results. It seems that in the frame of the individualized therapeutical approach of the infertile patients, the recombinant LH is an additional choice in the armamentarium of the IVF specialists.
**Infertility Treatment in the Environment of Economic Crisis: The Value of Pharmaco-Economics**

N. Maniadakis

**Objective:** To compare Gonal-F®, a recombinant follicle stimulating hormone (rFSH), with (Menopur®), a highly purified human menopausal gonatotrophin (hpHMG) used in assisted reproduction in Greece.

**Method:** A decision tree in combination with a Markov model was adapted to assess the clinical and economical impact of comparators for up to three consecutive cycles. Transition probabilities for all stages of a treatment cycle (i.e. cancelled ovum retrieval, successful recovery of oocytes, fertilization of oocytes etc) were derived from literature and validated by clinical experts. Cost components such as “initial treatment cost”, “cost of oocytes”, “cost of needle puncture”, “cost of fertilization”, “cost of transfer”, “cost of cryo” and “cost of FET thawing” were derived from the electronic databases of selected private and public clinics. The average number of units used per cycle and the rate of adverse events were based on the literature. Drug prices and reimbursement tariffs, were obtained from the “Government Gazette” and valued at 2011 prices. A probabilistic sensitivity analysis was performed to deal with uncertainty and to construct a cost-effectiveness acceptability curve.

**Results:** There was a statistical significant difference in favor of the rFSH arm compared to hpHMG, which is associated with 52 more births (95%UI: 26-78, p:0.001) per 1,000 patients. The cost per birth was estimated at €16,906 (95%UI: €16,347 – €17,516) and €17,286 (95%UI: €16,740 – €17,845) in the rFSH and hpHMG arms, respectively. The cost per IVF was estimated at €4,365 (95%UI: €4,205 – €4,506) in the rFSH and €3,815 (95%UI: €3,661 – €3,953) in the hpHMG arm, indicating a difference at €550 (95%UI: €365 – €730, p: 0.001). The incremental cost per birth for rFSH versus hpHMG was estimated at €14,540 (95%UI: €10,509 – €21,868), while the incremental cost per life year was estimated at €175.41 (95%UI: €163.44 – €213.17).

**Conclusion:** rFSH may represent a cost-effective choice compared with a hpHMG used for ovarian stimulation in the Greek NHS setting.

---

**SESSION IV SURGICAL TREATMENT**

**Surgical management of endometriomas: vaporization or cystectomy?**

A. Watrelot  
Hôpital NATECIA, Lyon France

Many works today have clearly demonstrated the superiority of cystectomy on vaporization/coagulation in case of endometriomas. Indeed vaporization is easier than cystectomy but today operative laparoscopy makes cystectomy always possible.

The question remains: is it always the best option? Because if the superiority of cystectomy is established in term of risk of endometriosis recurrence, it is less clear in term of ovarian function preservation.

It seems therefore important to decide according to the size, the number and the localisation of the endometriomas.

Also in case of vaporization, it is important to discuss the type of energy used.

At the end it is probably necessary to propose a mitigated attitude in which, patient equipment and surgical skills are probably important parameters.
Laparoscopic nerve-sparing surgery of deep infiltrating endometriosis: description of the technique and patients’ outcome

A. Kavallaris, M.D., PhD.
Department of Obstetrics and Gynaecology, University of Schleswig-Holstein, Campus Luebeck, Germany
4th Department of Obstetrics and Gynecology, Aristotle University of Thessaloniki, Greece

Endometriosis is understood as the heterotopic occurrence of tissue, which is morphologically and functionally similar to the endometrial tissue of the uterine cavity. Deep infiltrating endometriosis can cause chronic pelvic pain that often has not only a profound impact on a woman’s personal health and quality of life, but also an economic impact through loss of working hours [1], non-menstrual pain, deep dyspareunia or dyschezia. The average operating time was 82 min (range 45–185). Frequently, deep infiltrating endometriosis is found at the level of the rectovaginal septum and the uterosacral ligaments in the posterior pelvic wall, close to the nerves. Pain caused by or related to the disease is probably also due to neural infiltration [2]. The pelvic autonomic nerves are the pathway for the neurogenic control of rectal, bladder, and sexual arousal (lubrication and swelling of the vagina). The inferior hypogastric nerves carry the sensitive fibers and the sympathetic fibers responsible for the relaxation of the bladder detrusor muscle and contraction of the urethral sphincter. The pelvic splanchnic nerves carry the parasympathetic fibers, which are responsible for the voiding function of the detrusor of the bladder. The radical surgery of the deep infiltrating endometriosis of the rectovaginal septum and the uterosacral ligaments with or without bowel resection can cause serious damage of the pelvic autonomic nerves with urinary retention and the need of self-catheterization for a long period or even permanently [3–6]. Even single-sided radical dissection of the uterosacral ligaments with injury of the nerves can induce important urinary retention [3]. Different nerve-sparing techniques have been adapted in radical surgery for early cervical cancer [7–11]. Although the anatomy of the pelvic autonomic nerves is not fully described, we believe that laparoscopy allows better visualization of the retroperitoneal structures and better identification of important nerve structures of the pelvic autonomic nerves. It is especially due to the enlargement achieved by the modern video-optical systems with digital zoom function and carbon dioxide pressure.

The surgical procedure of the laparoscopic nerve-sparing resection of endometriosis was performed under general anesthesia in a Trendelenburg position, with the four-port laparoscopy performed after the pneumoperitoneum has been created with a Veress needle. One 11 mm port was inserted through the umbilicus for camera introduction and a 5 mm port inserted suprapubically. Two lateral 5 mm ports were inserted lateral to the visualized inferior epigastric vessels. The whole abdominal cavity, including peritoneum, liver, gall bladder, stomach, appendix, and bowels was inspected for pathologies. After bringing the patient in a head-down position, bowels were moved out of the pelvis and the inner genital organs were inspected. The identification of the inferior hypogastric and the splanchnic nerves was always performed independently when isolated resection of the uterosacral ligaments only or resection of the lateral pelvic wall was performed.

A single identification of the inferior hypogastric and the splanchnic nerves was performed when a single-sided resection of the uterosacral ligaments or single-sided resection of the lateral pelvic wall was needed to perform. We used a different approach of the nerves identification as the majority of the authors [3, 4, 9, 11, 12,13,14] who described their technique of the laparoscopic nerve-sparing procedure. The procedure of nerve identification started with the identification of the ureter at its crossing with the common iliac artery. We opened the peritoneum 1–2 cm medially of this junction. We then started with the preparation towards the promontory until the lateral part of the plexus hypogastric superior was visualized.
The superior hypogastric plexus is a triangular-shaped net of sympathetic fibers that lies in presacral space at the level of promontory, covered by peritoneal sheet, and the anterior layer of the visceral pelvic fascia. It gives origin to the right and left inferior hypogastric nerves, descending for 8–10 cm along the lateral sides of mesorectum, into the bilayered visceral pelvic fascia, following the ureteral course in a dorsal and caudal direction. After the identification of the inferior hypogastric nerve, we started with the preparation of the nerve towards the uterine artery with simultaneous removal the inferior hypogastric nerve away from the uterosacral ligament. The inferior hypogastric nerve appears approximately 2–3 cm dorsally of the ureter in the lateral part of the uterosacral ligament when entering the lateral parametrium (Fig. 1). The pelvic splanchnic nerves run from the S2–S4 roots of the sacral plexus and join in the inferior hy-
pogastric plexus with the inferior hypogastric nerves at the lateral part of the uterosacral liga-
ments (Fig. 2), laterally to the rectum at the level and dorsal of the cardinal ligament. The infe-
rior hypogastric plexus forms a "triangularly shaped plexus, placed in a sagittal plane" [8]. After
the identification of the inferior hypogastric nerve and the splanchnic nerves, we performed
the radical resection of the all structures infiltrated by endometriosis.

The median BMI was 23.5 (range 17.26–28.04). The average operating time was 82 min (range
45–185). There were no intra- or post-operative complications and the approximately blood loss
diVerence was 250 ml (range 120–300). In all patients, at least a single-sided resection of the
uterosacral ligament was performed. Dysmenorrhoea, pelvic pain, and dyspareunia disappeared
postoperatively in all patients. Bladder bleeding in two patients with bladder endometriosis,
conﬁrmed by biopsy prior to surgery, disappeared postoperatively. Postoperatively, except the
three patients with bladder and ureter resection, in all the other patients, spontaneous voiding
was possible on the ﬁrst postoperative day with a median residual urine volume of <50 ml. For
patients with bladder and ureter resection, a diVerent postoperative management was per-
formed. After the removal of the Foley’s catheter, all three patients were able to have sponta-
neous voiding (two patients with bladder resection on 7 postoperative day and the patient with
ureter resection on 9 postoperative day) with no urinary retention.

Overall the time to resume voiding function was two postoperative days and the residual urine
volume was in all patients <50 ml in two ultrasound measurements.

Identification and preservation of the nerves are not always feasible, but a procedure sparing
the nerves is advisable since radical surgery in endometriosis can lead to some long-term blad-
der dysfunction such as urine retention. We think that enlargement of the laparoscopic view
using modern video-optical systems with digital zoom function helps for better visualization of
the nerves especially of the single fibers of the inferior hypogastric plexus. However, we be-
lieve that some experience is needed to visualize the nerves, but the knowledge of their pres-
ence is the most important factor for their preservation.

Laparoscopic identiﬁcation (neurolysis) of the inferior hypogastric nerve and inferior hypogas-
tric plexus is a feasible procedure for trained laparoscopic surgeons who have a good knowledge
not only of the retroperitoneal anatomy, but also of the pelvic neuro-anatomy as this qualiﬁca-
tion could prohibit long-term bladder and voiding dysfunction.

References
ship between endometriotic foci and nerves in rectovaginal endometriotic nodules. Hum
Reprod 15:1744–1750
with deep infiltrating endometriosis. Surg Endosc 18(7):1109–1112
Zanolla L, Minelli L (2006) Laparoscopic nerve-sparing complete excision of deep end-
dometriosis: is it feasible? Hum Reprod 21(3):774–781
surgical resection of deeply infiltrating endometriosis: pathophysiology and management.
Gynecol Obstet Fertil 35(Suppl 1):S8–S13 (Review in French)
effects after surgery for deep pelvic endometriosis. Gynecol Obstet Fertil 35(Suppl 1):S1–S7
(in French)
radical hysterectomy: oncologic rationale, surgical anatomy, and feasibility study. Am J Ob-
stet Gynecol 178:971–976
pelvic autonomic nerves. Lancet 354:772–773
Hysteroscopy and Adenomyosis

Dr. Rudi Campo
LIFE, Leuven Institute for Fertility and Embryology, Tiensevest, 168, 3000 Leuven, Belgium

Adenomyosis, the heterotopic presence of endometrial glands and stroma within the myometrium, has traditionally been diagnosed by the pathologist in hysterectomy specimens. However, the recent development of high quality non-invasive techniques such as transvaginal sonography (TVS), magnetic resonance imaging and office mini hysteroscopy with the Trophy hysteroscope, with the possibility of directed tissue sampling of the myometrial layer, has renewed the interest in the diagnosing and treatment of adenomyosis.

The use of MRI can be considered as a turning point in the appreciation, not only of adenomyosis as a disorder of the female reproductive tract, but also in the appreciation of the subendometrial junctional zone. But as MRI cannot be implemented as a screening tool, we will discuss the value of the integrated Ultrasound – hysteroscopic approach to diagnose and treat adenomyosis.

The TROPHYSCOPE is a compact very thin hysteroscope with an outer diameter of only 2.9 mm which does not require any assembling in its single-flow version. An innovative feature of this hysteroscope is that it can be loaded with an accessory sheath providing several accessory functions. One interesting function is that it can serve as a guide for the Spirotome, a device made to harvest high quality samples from soft tissues. It is built on the pioneering concept of a cutting helix on a cutting cannula well identified by Ultrasound. The sample is harvested by turning the helix into the diseased area under ultrasound guidance. The cannula turns subsequently over the helix to free the sample from the surroundings.

Although diagnostic hysteroscopy do not provide pathognomonic signs for adenomyosis, some evidences suggest that subtle lesions, like irregular endometrium with endometrial defects, altered vascularisation and cystic haemorrhagic changes, are possibly associated with the entity. In addition to the direct visualization of the uterine cavity, the approach with the Trophy hysteroscope offers the possibility to obtain immediate endometrial/myometrial tissue. Since they can be performed in the office or in the ambulatory unit, the combination of TVS, fluid hysteroscopy and contrast sonography are therefore powerful screening tools for detecting endometrial and myometrial abnormalities in association with adenomyosis.
Endometriosis and Miscarriage: Is there any association?

Marco Gergolet MD

Septate uterus is commonly recognized as one of the main factors causing pregnancy loss or premature delivery. In studies done on general population, a significant convergence of history of recurrent miscarriages and of preterm delivery with the presence of a uterus septus or bicornis has been found (Maneschi et al., 1995). Metroplasty dramatically improves the pregnancy outcome with a concomitant decrease of the miscarriage rate and an increase in term deliveries (Doridot et al., 2003, Paboccu and Gomel 2004). A correlation between endometriosis and spontaneous miscarriage has been reported by different studies (Metzger et al. 1986, Olive et al. 1982), but a direct correlation between the miscarriage rate and severity of endometriosis has never been proven (Pittaway et al. 1988). Several authors report a decreased miscarriage rate after surgical therapy of endometriosis (Wheeler et al. 1983, Donnez et al. 2002), whereas other did not find any difference (Matorras et al. 1998, Parazzini et al. 1999). Recent studies correlate non-obstructive Mullerian anomalies, such as uterine septa, with an increased incidence of endometriosis. Nawroth observed a higher incidence of endometriosis in women with non obstructive forms of Mullerian anomalies like septate uterus: in a retrospective study 120 women with a septate uterus were compared with 486 infertile women with a normal uterus, assessed by hysteroscopy and laparoscopy. The incidence of dysmenorrhea was similar in the two groups whereas the incidence of endometriosis was higher (25.8%) in the group of patients with septate uterus, comparing the group with a normal uterus (15.2 %). The hypothesis, referring also to other authors (Leydenecker et al 2004) is that abnormal uterine peristaltic waves could lead to peritoneal colonization of endometrial stem cells (Nawroth et al. 2006).

The aim of the study was to verify whether hysteroscopic metroplasty of uterine septa could be advantageous in term of reduction of miscarriage rate in a group of patients with endometriosis.

Materials and Methods: 246 women underwent a hysteroscopic metroplasty from Jan 2000 to Dec 2005 due primary or prolonged secondary infertility or after one or more pregnancy failures. Cases with male factor of infertility, bilateral tubal factor and patients with uterine septum who did not want to conceive after the metroplasty were excluded from the study (179 out of 246 were included). 36 women out of 179 had I. and II degree endometriosis. We compared the pregnancy outcome of the septum with endometriosis group before and after metroplasty to the pregnancy outcome of the septum without endometriosis group (143 women with septum but without endometriosis).

Results: The two groups were homogeneous for age (29,62 +/- 4,5 years in endometriosis group vs. 29,41 +/- 4,84 years in non endometriosis, BMI (21,73 +/- 3,28 vs. 21,63 +/- 3,11), and obstetric history (37,5 % vs. 49,7 % of secondary infertility).

Before metroplasty the incidence of spontaneous abortion in the septum with endometriosis group was 75 %, in the septum without endometriosis was 67% (P=0.68, n.s.). After metroplasty 16 women (44,4 %) from the septum with endometriosis group and 47 women (32.9 %) from the septum without endometriosis group did not conceive (n.s.). The incidence of pregnancy failure (abortion and ectopic pregnancy) in the septum with endometriosis group was 19,4 % (7 women), in the septum without endometriosis group 12 women did not achieved a full term pregnancy (8.4%) (n.s.). 29 women from the septum with endometriosis group (80,6 %) and 131 women from control group (91.6) delivered at term.

Conclusions: In our study increased abortion rate depends more likely on uterine malformations than on endometriosis. Endometriosis seems to be an occasional finding not influencing on pregnancy outcome.
Oral contraceptive pills for the treatment of Endometriosis

P. Inaudi
Dpt. Of Pediatrics, Obstetrics and Reproductive Medicine, University of Siena, Italy
inaudi1@interfree.it

Endometriosis is a gynecological disease of unknown etiology, affecting women during the reproductive life. Medicalization and impaired quality of life have an important economic impact for women and society. Considering that the disease cannot be cured, the goal of the treatment is then aimed to reduce symptoms and endometriotic lesions, to achieve a better quality of life. The most frequent symptoms of endometriosis are isolated or multiple ovarian cysts, pelvic pain and infertility and then the treatment should be performed in order to reduce the entity of the symptoms and to prevent a further development of the disease.

Oral contraceptives (OC) have been used for more than fifty years based on the observation that pregnancy, which is characterized by very high concentrations of estrogens and progesterone, is associated with a marked reduction or disappearance of the endometrial lesions. In order to realize a pseudo-pregnancy, different composition and amount of OC were given; nevertheless, a low-dose contraceptive pill is equally effective than the administration of 2 or more pills per day, in reducing the symptoms associated with endometriosis. OC are equally effective also when compared with the GnRH analogues which are able to totally suppress hormonal production by the ovary and consequently block the stimulation on endometriotic lesions. Either estrogens + progestins or progestins alone are widely used in order to improve the condition. The progestin-induced anovulatory status is responsible of decidualization and atrophy of the endometrial tissue. The induction of cell death and reduction of endometrial cells proliferation are some of the positive actions of OC; nevertheless, the lesion can remain at the minimal, but sensitive, stage, ready to re-start its activity in appropriate conditions.

Different formulations of OC have been demonstrated to be able to control symptoms, mainly pain, of endometriosis. Recently, Dienogest, a synthetic progestin, has been investigated; 2 mg daily, effectively alleviates pain and follow-up, after suspension of the treatment, shows an acceptable pain-free period.

OC treatment should be viewed as a first line treatment in those women not wishing to conceive while in those that want a pregnancy other treatments must be considered. Actually, the OC has not a positive impact on endometriosis-related infertility, while, the inhibition of ovulation exclude the possibility of a pregnancy.

The use of OC can be then used as a first line treatment or after other treatments, like GnRH analogs or surgery, with the aim of reducing the amount of retrograde menstrual blood and uterine contractions, so obtaining a less painful condition in order to achieve an acceptable quality of life limiting the progression of the disease and reduction of symptoms.

Should we treat endometriosis before in-vitro fertilization?

Professor Basil C. Tarlatzis, MD, PhD
Director of 1st Dept of OB/GYN, School of Medicine, Aristotle University of Thessaloniki, “Papageorgiou”, General Hospital Greece

Endometriosis represents one of the most important gynecological conditions in women of reproductive age. It is identified in 10-25% of subfertile couples, although the mechanism with which it reduces the chance of spontaneous conception remains mostly unknown. It has been suggested that in the presence of endometriosis the probability of pregnancy after IVF decreases approximately by half. This is accompanied by a significant decrease in the number of oocytes retrieved, fertilization and implantation rates.
The optimal treatment for subfertile women with endometriosis is a matter of debate, since data from relevant randomized controlled trials are currently scarce. Generally, women wishing to conceive are treated by IVF or subjected to medical/surgical treatment and expected management. Whether endometriosis should be treated before the initiation of an in-vitro fertilization (IVF) cycle has been a matter of debate for many years and has led to several relevant publications. Medical treatment for IVF has so far included oral contraceptives, progestins, prolonged GnRH analogue treatment, danazol and gestrinone. Evidence derived from randomized trials, prospective and retrospective trials suggests that pregnancy rate per cycle is significantly increased after prolonged GnRH analogue treatment prior to IVF. No data currently exist on the use of GnRH antagonists for the same indication. On the other hand, the limited data, regarding pretreatment of these patients with danazol or gestrinone, do not support a beneficial effect in terms of pregnancy rates after IVF. Furthermore, existing evidence does not support a beneficial effect of excising endometriomas immediately prior to IVF, while the optimal method of excision is still debatable.

In conclusion, with the exception of the use of prolonged GnRH agonist treatment, none of the treatment modalities seems to be associated with an increase in the probability of pregnancy after IVF in patients with endometriosis.

****

**Fertility Preservation option in patients with severe Endometriosis**

**Stratis Kolibianakis MD MSc Phd**

One of the most common problems associated with endometriosis is pelvic pain. Treatment in most cases involves ablation of endometriotic implants or excision of ovarian endometriomas. Despite the experience of the treating surgeon, however, such an approach may decrease ovarian reserve. In fact, bilateral excision of endometriomas has been associated with immediate initiation of menopause in a small proportion of women with endometriosis. Although the natural history of endometriosis remains largely unknown, the endometriotic cysts themselves may result in structural tissue alterations that contribute to a decreased ovarian reserve. Not surprisingly, it is well established that the chance of pregnancy in women with endometriosis-associated infertility undergoing IVF is decreased by half and that the number of oocytes retrieved as well as fertilization rates are significantly decreased compared with women with no endometriosis. Considering the above, it is clear that in a proportion of patients with endometriosis, who wish to become pregnant in the future, the need for considering fertility preservation options is appropriate.

Fertility preservation comprises of several rapidly evolving techniques. Although these were originally offered to cancer patients, they may also help women in whom their fertility potential is at risk, as is the case with patients suffering from endometriosis. However, due to the fact that the rate of oocyte depletion may vary between women diagnosed with endometriosis, it may not be easy to determine how early to offer fertility preservation. In this respect, determination of ovarian reserve by assessing antral follicle count, serum levels of FSH and AMH might be useful.

The only established method of fertility preservation in women today is embryo cryopreservation. In patients with endometriosis, who are being treated by IVF, embryo cryopreservation remains an option for preserving future fertility. This might be significantly decreased, when the couple seeks treatment again, following the delivery of their first baby conceived after IVF. However, embryo cryopreservation might not be an option in a significant proportion of patients with endometriosis because they either lack a male partner, or they do not wish to cryopreserve embryos for religious or moral reasons. In this case, oocyte cryopreservation can be offered. Recent improvements in cryopreservation methods, with the advent of vitrification, have significantly increased the effectiveness of oocyte cryopreservation. Oocyte cryopreservation is usually performed at the metaphase II stage. Cryopreservation of immature oocytes at the GV stage has not been very successful until today. The use of ovarian tissue cryobanking remains experimental and the number of live births reported following from transplantation of cryopreserved ovarian tissue remains limited.
Ovarian endometriomas derange the physiological mechanisms of ovulation. In presence of advanced endometriosis not only lower number and quality of oocytes achieved but also lower implantation rates have been reported. Mechanical and vascular effect of endometriotic adhesions may decrease the number of M2-oocytes retrieved in IVF. Gonadal damage is at least partly initiated by the presence of endometriotic cells per se preceding surgery causing local inflammation, creation of adhesions and destruction of microvascularization.

Infertility cases main concern is the choice of treatment, medical or surgical or combined. Considering endometriosis as a spontaneously regressive phenomenon, the risk of recurrence rate is high, hence the synchronization of remission and treatment is crucial for achieving a pregnancy. The results of in-vitro fertilization with advanced endometriosis are lower as compared to those that appropriate surgery was performed prior to IVF. The old opinion that whatever type of surgery is performed the IVF results are not impaired if ovarian cortex stays intact is wrong. The destruction of normal ovarian tissue increases with the persistence of endometriosis and larger the size of endometriomas or implants. Also the number of endometrioma cysts and extend of the disease reduces the pregnancy rate (PR). The rate of ovulation found to be 35% when one endometrioma cyst and 19% when 2 cysts were present, while the size of more than 30mm reduces significantly the PR.

The delay of first baby in the family planning of modern women over the age of 30 and 35 created more cases with advanced endometriosis and comorbidity. Surgery for minimal or mild endometriosis is debated due to modestly enhance fecundity in women with otherwise unexplained subfertility. Conflicting information may be due to the fact that endometriomas are mostly unilateral and most of these women, finally they do get pregnant. Probably a consensus will never be reached on the optimal treatment of minimal and mild endometriosis. Efficacy of medical and surgical treatment of endometriosis in infertility is an ongoing controversy. In addition we must take in consideration that there are no tools to predict who will progress to severe disease. Complete resolution of endometriosis is not yet possible and current therapy targets to reduce pain, to increase the possibility of pregnancy and to delay recurrence for as long as possible.

In cases of moderate and severe endometriosis-associated infertility, the combined laparoscopic surgery with GnRHa may be the ‘first-line’ treatment. The mean PR of 50% following surgery provides scientific proof that reproductive surgery should first be the first choice in order to give patients the best chance of conceiving naturally. In cases with large endometriomas >6cm, the ovarian reserve determined by AMH is less diminished after three-step procedure. The ovary is explored to determine the extent of disease. Dark, punctuate lesions beneath the cortical ovarian surface give the orientation of the location of the disease. Adhesion formation could compromise distal tubal function. Inability to elevate the ovary is usually a sign of adhesions and endometriotic implants of the inferolateral surface of the ovary and the peritoneum of the ovarian fossa. Filmy adhesions are elevated with delicate tissue forceps and can resected with fine-needle cautery, a scalpel or laser. Maintain the integrity of the ovarian capsule. Peritoneal spillage of the contents of the endometrioma can and should be avoided. During the cortical incision preserve the normal anatomic relations of the ovary with the uteroovarian ligament and fimbria ovarica. A shallow longitudinal incision over the endometrioma with the monopolar microneedle, scalpel, or laser is a good option. Facilitate creation of a cleavage plane between the cyst and normal ovarian tissue. Eliminate the dead space and maximize hemostasis. Minimize thermal injury to surrounding ovarian tissue and near the fimbria ovarica. The experience and the skills of the surgeon as well as the strict selection of the patients seem to be important to achieve pregnancy.
Altermon®
Highly Purified FSH

Merional®
Human Menopausal Gonadotrophin

FARAN LABORATORIES s.a.
IBSA
Κοίτα τα αριστουργήματα που δημιουργούμε μαζί

Merck Serono | Εσείς, Εμείς. Μαζί είμαστε οι γονείς της γονιμότητας.

Merck Serono | Living science, transforming lives