

Feelin' stronger every day*

Dear Friends,

During the Montpellier meeting, the WES Board decided to appoint a number of Ambassadors of our society.

What is an Ambassador?

According to Wikipedia, "the word is also often used more liberally for persons who are known, without national appointment, to represent certain professions, activities and fields of endeavor."

Why WES Ambassadors?

The endometriosis scientific community has particular characteristics.

On the one hand it has an enormous scientific and "political" potential, as it includes so many capable, authoritative, and highly motivated researchers and clinicians. On the other hand, however, it looks fragmented into several smaller sections, such as national societies or special interest groups, somewhat diverting the main river water flow into a myriad of creeks.

We believe that coordinating these multiple dispersed efforts could result in a powerful organised group capable of supporting novel ideas, influencing the decisions of health-care providers, and increasing the social awareness of the disease.

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A/Professor Paolo Vercellini
WES President

The World Endometriosis Society, uniquely, has the ability to collate worldwide activities and to concentrate these broadly distributed forces into a principal, much more powerful vector.

Achieving a powerful vector

We can reach this goal by establishing a network of influential scientists and clinicians dedicated to the dissemination of information by our society, by focusing on our global approach to the disease, by collecting new notions to be addressed in our world congresses, and by creating a mutual intellectual exchange as well as practical support between WES, local societies, and international special interest groups.

What do we expect from WES Ambassadors?

Hopefully, our Ambassadors, just as our members, will feel the sense of belonging to our community and will recognise WES as the reference society for those of us involved in research in and management of endometriosis – and will encourage their colleagues, with an interest in endometriosis, to become engaged in our global community as well.

We expect Ambassadors to raise awareness of the disease, foster research, mentor colleagues to become engaged in this global community, and promote our triennial meetings. This is particularly important in those countries where endometriosis is still poorly

known, diagnosed, and treated, leaving a multitude of women agonising in pain with limited hope of receiving concrete help.

Moreover, several of our newly appointed Ambassadors also cover key roles in national and international societies. We invite them to facilitate interaction between these organisations and WES in terms of both scientific projects, such as common guidelines or research programmes, and exchange invitation of speakers in respective meetings.

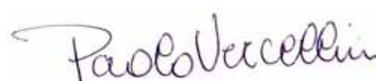
Finally, we hope that our Ambassadors will disseminate throughout the world our thoughts and positions, which have been synthesised in Montpellier during the one-day pre- and post-congress workshops on, respectively, research directions, and diagnosis and management of endometriosis.

Ambassadors and future plans

After a long process, the WES Board finally agreed on a list of more than 40 influential members: <http://endometriosis.ca/about/ambassadors/>, who are

working with, training, and/or inspiring a multitude of other colleagues around the world engaged in researching and treating endometriosis – colleagues whose efforts are also greatly valued and essential for the creation of this powerful vector!

All the activities described above will be developed on a voluntary basis. We believe that establishing the position of “WES Ambassadors” constitutes an important step for the future development of our organisation and are grateful to those who have accepted to serve our society. So, let’s now build the world endometriosis network together!



Paolo Vercellini
President
World Endometriosis Society

*by Cetera P, Pankow J. Chicago. In: Chicago VI, Columbia Records, USA, 1973.

Upcoming meetings

Joint ASRM/ESHRE pre-congress course on “Endometriosis and pain”	1 July 2012 Istanbul, Turkey
28th Annual Meeting of ESHRE	1 – 4 July 2012 Istanbul, Turkey
4th Congress of the Asia Pacific Initiative on Reproduction (ASPIRE 2012)	30 August – 2 September 2012 Osaka, Japan
21st Annual Congress of the European Society for Gynaecological Endoscopy	11 – 14 September 2012 Paris, France
XX FIGO World Congress of Gynaecology and Obstetrics	7 – 12 October 2012 Rome, Italy
2012 Annual IPPS Fall Meeting on Pelvic Pain (International Pelvic Pain Society)	18 – 21 October 2012 Chicago, USA

A word from the editor

Welcome to the latest edition of the WES eJournal. Over the last couple of weeks, some very significant events have happened around the world: Greece is stuck with a hung parliament, Sarkozy is the first French president in a long time not to get re-elected, and Obama has spoken out in support of gay marriage. In this edition we are proud to announce some further events, similarly important of course, but admittedly not with the same global relevance.

As always our President opens the eJournal. As mentioned in his inaugural address in Montpellier, he has launched an initiative to broaden the reach of WES through the appointment of a number of WES Ambassadors. Read his contribution to learn more.

This edition's guest editor contribution comes from WES Board Member Dr Rishma Pai. She gives an overview of the use of ART in women with endometriosis. I am sure you will enjoy the review and the many useful references.

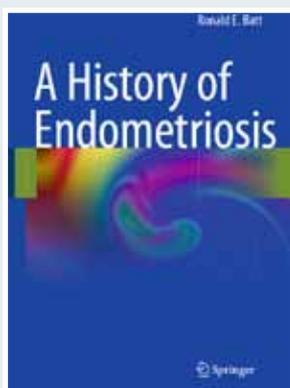
Professor Mauricio Abrao will be the proud host of the next World Congress of Endometriosis in Sao Paolo in 2014. He is already hard at work making sure the congress will be a great success. In this issue Mauricio talks about another new initiative of the WES board. The ultimate success of the tri-annual meetings depends largely on your contributions. WES has always emphasised the abstract-driven format of the conference. As such, all stakeholders and interest groups within the field of endometriosis-research must feel represented. So, for the first time, you will be given the opportunity to help shape the congress programme. Please read Mauricio's announcement of this important initiative on [page 15](#) and have your say!

Last but not least, the editorial office is very pleased to have received a letter in response to Paolo Vercellini's contribution in the last eJournal. We encourage WES members to follow Professors Brosens' and Putteman's example and to be more actively involved in the eJournal as well.



A/Professor Luk Rombauts
WES eJournal Editor

Are you serious about endometriosis?



Then you must read *A History of Endometriosis* to make sure you know everything there is to know about the disease! Ronald Batt MD takes us on a scientific (and entertaining!) journey from the early science of endometriosis leading to today's understanding of the disease.

Each chapter entertains with remarkable insight into not only the work of all the early pioneers, but also the environment that shaped each revelation upon which we are continuing to build of understanding of this complex disease today.

A History of Endometriosis can be **purchased online** and all royalties are being donated by Dr Batt to the **Rodolphe Maheux Travel Fund for Young Scientists**.

ART and Endometriosis

Dr Rishma Pai MD[1], Dr Nandan Roongta DNB[2], Dr Hrishikesh Pai MD[3], Dr Nandita Palshetkar MD[4]

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Introduction

The clinical association between endometriosis and infertility, though uncertain to start with, has been better defined over the past few decades. It is estimated that during the reproductive years about 6-10% of the general female population is affected by endometriosis. And 30-50% of these women are sub-fertile. Approximately 20% of infertile women have endometriosis, ie. the presence of functional endometrial glands and stroma outside the uterine cavity (1). Pathologically, the condition could be clinically evident as microscopic foci to large haemorrhagic cysts and stellate pigmented patches in the peritoneal cavity, endometriotic cysts within the ovaries, or fibrosis and subsequent adhesions between involved tissues potentially leading to distortion of the uterus, obliteration of the pouch of Douglas and small bowel adhesions (3).

Pathophysiology

The exact pathophysiology underlying infertility in the presence of endometriosis is poorly understood. Anatomic distortion created by scarring and adhesions offers a clear mechanism for reduced pregnancy rates. However, in the absence of anatomic distortion, the cause of reduced fecundity is uncertain, possibly



Dr Rishma Pai
WES Board Member

involving hormonal disruption, local inflammation, altered immune response and/or other unknown mechanisms, leading to impaired uterotubal transport of sperm, disturbed ovulation, subtle impairment of oocyte and embryo quality, implantation defects, anti-endometrial antibodies, progesterone resistance, and an increased risk of recurrent miscarriage (2). This article attempts to highlight the various aspects of Assisted Reproductive technologies (ART) treatment in cases of endometriosis.

Diagnosis and Staging

Primarily, diagnostic laparoscopy with histologic examination of excised lesions is considered the 'gold standard' test for the diagnosis of endometriosis, since it permits direct visualisation and tissue biopsies. Disease extent is usually staged using the 1996 Revised American Society for Reproductive Medicine Classification of Endometriosis (5).

Stage of the disease is divided into:

Stage I (minimal): score 1-5

Stage II (mild): score 6-15

Stage III (moderate): score 16-40

Stage IV (severe): score > 40

Clinical evaluation and prognosis assessment is assisted by peripheral biomarkers (4) (commonly used are CA125, Interleukin-6, and the neutrophil-lymphocyte ratio), along with ultrasonography (detection of ovarian endometriomas or 'chocolate cysts' which may be

unilateral or bilateral), are secondary methods of diagnosis and prognostic evaluation.

The Endometriosis Fertility Index (EFI) (6)

The American Society for Reproductive Medicine classification system, aims to investigate the type and severity of endometriosis, and is unable to predict clinical outcomes such as pregnancy rate.

However, a new validated staging system, the Endometriosis Fertility Index (EFI) proposed in 2009, incorporates historical, surgical, and functional data to assign a score (Figure 1).

**ENDOMETRIOSIS FERTILITY INDEX (EFI)
SURGERY FORM**

LEAST FUNCTION (LF) SCORE AT CONCLUSION OF SURGERY

Score	Description	Left	Right
4	= Normal	<input type="checkbox"/>	<input type="checkbox"/>
3	= Mild Dysfunction	<input type="checkbox"/>	<input type="checkbox"/>
2	= Moderate Dysfunction	<input type="checkbox"/>	<input type="checkbox"/>
1	= Severe Dysfunction	<input type="checkbox"/>	<input type="checkbox"/>
0	= Absent or Nonfunctional	<input type="checkbox"/>	<input type="checkbox"/>

To calculate the LF score, add together the lowest score for the left side and the lowest score for the right side. If an ovary is absent on one side, the LF score is obtained by doubling the lowest score on the side with the ovary.

Lowest Score	<input type="checkbox"/>	+	<input type="checkbox"/>	=	<input type="text"/>
	Left		Right		LF Score

ENDOMETRIOSIS FERTILITY INDEX (EFI)

Historical Factors			Surgical Factors				
Factor	Description	Points	Factor	Description	Points		
<u>Age</u>	If age is ≤ 35 years	2	<u>LF Score</u>	If LF Score = 7 to 8 (high score)	3		
	If age is 36 to 39 years	1		If LF Score = 4 to 6 (moderate score)	2		
	If age is ≥ 40 years	0		If LF Score = 1 to 3 (low score)	0		
<u>Years Infertile</u>	If years infertile is ≤ 3	2	<u>AFS Endometriosis Score</u>	If AFS Endometriosis Lesion Score is < 16	1		
	If years infertile is > 3	0		If AFS Endometriosis Lesion Score is ≥ 16	0		
<u>Prior Pregnancy</u>	If there is a history of a prior pregnancy	1	<u>AFS Total Score</u>	If AFS total score is < 71	1		
	If there is no history of prior pregnancy	0		If AFS total score is ≥ 71	0		
Total Historical Factors			Total Surgical Factors				
EFI = TOTAL HISTORICAL FACTORS + TOTAL SURGICAL FACTORS:			<input type="text"/>	+	<input type="text"/>	=	<input type="text"/>
			Historical		Surgical		EFI Score

ESTIMATED PERCENT PREGNANT BY EFI SCORE

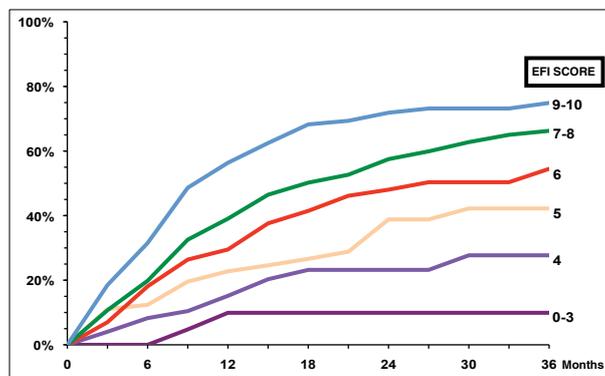


Figure 1: Endometriosis fertility index (EFI) scoring (6)

From Adamson and Pasha, Fertil Steril 2010;94(5):1609-15.

The EFI is a tool that can be used to help determine the prognosis and pregnancy rates, and hence optimal management following laparoscopy. Based on the prognosis, the length of time a patient should attempt natural conception post surgery can be predicted by the EFI.

- Surgical documentation of endometriosis is a prerequisite. The EFI staging system assesses the following key elements as a numerical measure:
 - **Functional anatomy:** based on careful assessment of the tubes (extent of serosal injury, mobility and patency), fimbriae (extent of injury, architecture) and ovaries (size, extent of surface injury).
 - **Co-factors:** Age, the duration of infertility, and the surgical aspects involved. To assess surgical difficulty and complications, Douglas obliteration, depth of bowel invasion, degree of hydronephrosis, and number of previous surgeries are important.
 - The EFI grades the condition from 0-10 (with 0 representing the poorest and 10 the best prognosis).
5. There are also guiding nomograms (42) which, like the EFI, help in assessing the prognosis and pregnancy rates in cases of endometriosis undergoing IVF-ICSI.

Infertility treatment in endometriosis

Treatment of infertility associated with endometriosis includes surgical methods, hormonal treatment, and assisted reproductive technologies (ART).

1. **Expectant management:** While surgery can address pain or anatomical distortion, it is of limited value in cases of minimal to mild disease, with the number needed to treat (NNT) for one extra pregnancy being about 7-8 endometriosis patients. Thus, in at least some young, otherwise-good prognosis patients with minimal to mild disease and no symptoms other than infertility, observation for 3-12 months is a reasonable option, often followed by 3-6 months of controlled ovarian stimulation with clomiphene citrate.
2. **Medical treatments** for endometriosis are contraceptive as such. However in those desirous of conception, hormonal pre-treatment for ovarian

suppression, eg. 3-6 months of gonadotropin-releasing hormone analogues—improves the outcome of ART (16).

3. **Ovarian stimulation with intrauterine insemination:** Used in the good-prognosis patients, with minimal to mild endometriosis as the only diagnosed factor contributing towards the subfertility.
4. **Surgical methods:** As per ASRM and ESHRE guidelines (9,10) disease confirmation is typically the indication for the initial laparoscopy, and often is the point of initial surgical ablation of visualised lesions. However, repeated laparoscopic surgeries can catalyse scarring and adhesion formation and may diminish ovarian reserve (11,12).
Laparoscopy offers improved visualisation, reduced tissue trauma and reduced new adhesion formation, as well as quicker recovery, compared with laparotomy. Different laparoscopic techniques for the destruction of endometriosis lesions are equivalent, surgical expertise being the most important technical determinant of outcome. Data, indicate that surgery at any stage of endometriosis enhances the chances of natural conception. Surgery provides diagnostic information regarding the extent of disease and can treat both endometriosis lesions and the anatomic distortion caused by adhesions and scarring. Surgical management may also address multiple components of the reproductive process, such as immunobiological, inflammatory and other changes, thereby contributing to the increased spontaneous pregnancy rates after surgery.
In the presence of severe pain, most clinicians agree that surgical intervention is warranted, particularly given the impact that dyspareunia has upon spontaneous conception. When age, ovarian reserve, and male and tubal status permit, surgery should be considered immediately so that time is dedicated to attempts to conceive naturally.
 - Pre-operative ovarian suppression treatment: While there are some theoretical advantages of this, there are no data that conclusively show benefit.
 - Post-operative suppression treatment has been shown to be of no benefit.
 - Since repeat surgery is generally not effective, after 9 to 18 months, IVF becomes the best option for almost all patients.

During surgery: Moderate to severe endometriosis is most often associated with significant anatomic distortion and a low spontaneous pregnancy rate if left untreated. It is widely believed that surgical intervention with cyst wall removal, improves pregnancy rates by restoring anatomic relationships and reducing the impact of endometriosis lesions. The number and/or size of the endometriomas do not generally affect pregnancy rates, the most important factor being preservation of the maximum amount of viable ovarian tissue.

But prior to an ART cycle, with endometriomas, it is still not known whether cystectomy, especially for those less than 4cm in diameter, is beneficial in improving results. Criteria for non-removal of endometriomas pre-ART are: bilateral cysts, history of past surgery, and altered ovarian reserve.

5. **ART:** An “emergency” in vitro fertilization (IVF) procedure specific to women with endometriosis who were experiencing infertility was recently proposed. In brief, it detailed on prioritizing measurement of ovarian reserve and hysterosalpingogram evaluation of tubal patency (with inclusion of standard evaluation for indications of male infertility in the partner). If those parameters show alterations, surgical treatment would be avoided with immediate progression to IVF. They stressed this accelerated path to IVF is particularly critical among women older than 38 or those with infertility of long duration (2).
6. Weighing up the relative advantages of surgery, medical treatment and ART (8) are the foundations for a global approach to infertility associated with endometriosis.

ART in endometriosis

Endometriosis associated with infertility is most effectively managed by early aggressive treatment with IVF, with supporting pretreatment wherever it is deemed necessary. ART is able to bypass most of the endometriosis-related mechanisms of infertility in order to achieve a pregnancy, except for oocyte/embryo quality.

Pre-ART investigations in endometriosis

Specific among the other routine pre-ART investigations are:

- **Ovarian reserve:** Serum AMH may be a better predictor of the ovarian response of COH in patients with endometriosis than basal FSH or age. Also AMH level can be considered a useful clinical predictor of poor ovarian response in endometriosis patients (39).
- **USG:** A transvaginal ultrasound with colour doppler assessment would guide as to the exact location of ovaries and access to them during oocyte retrieval, the proximity to blood vessels or bowel, and the size of endometriomas if any. Antral follicle count can also be assessed.

Pre-ART treatment in endometriosis

7. **Surgery:** The classic, unproven dogma that ovarian endometrioma should be removed in all infertile women prior to IVF has been recently questioned. Fears that surgery can alter ovarian function that is already compromised sparked a rule of no surgery before ART (18). Convincing evidence has emerged showing that responsiveness to gonadotrophins after ovarian cystectomy is reduced. Conversely, the impact of surgery on pregnancy rates is unclear since no deleterious effect has been reported. The fact then is that surgery exposes women to risks related to a demanding procedure whereas risks associated with expectant management are mostly anecdotal or of doubtful clinical relevance. It has hence largely been recommended that proceeding directly to IVF to reduce time to pregnancy, to avoid potential surgical complications and to limit patient costs, is the better option. Surgery should be envisaged only in presence of very large endometriomas (balancing the threshold to operate with the endometrioma location within the ovary), or to treat concomitant pain symptoms which are refractory to medical treatments, or when malignancy cannot reliably be ruled out (7, 18) and in cases where there is a need to improve access for oocyte aspiration.
8. **GnRH analogues:** Their use prior to the ART is in order to reduce the endometrioma size. Whether prolonged treatment with GnRH agonists in women with endometriosis is significantly better than the long protocol for IVF is unclear and further studies are needed in this area.
9. **Oral contraceptives:** In women with endometriosis, including those with endometriomas, 6 to 8 weeks

of continuous use of oral contraception pills before assisted reproduction treatment maintains ART outcomes comparable with the outcomes of age-matched controls without endometriosis. In contrast, ART outcomes are markedly compromised in endometriosis patients who are not pretreated with OCPs. Ovarian responsiveness to stimulation was not altered by 6 to 8 weeks' use of pre-ART OCPs, including in poor responders with endometriomas (24).

10. Lifestyle: While no data currently exist regarding lifestyle alteration within endometriosis patients embarking on ART to maximize success, studies of the relation with endometriosis directly suggest that minimizing cigarette smoking and improving diet (increasing healthy fats and vegetables while minimizing unhealthy fats and red meat) may have a beneficial effect on the disease or its symptoms (13,14).

11. Multidisciplinary teams including endometriosis and ART specialists as well as complementary medicine, epidemiologists, and scientists must be formed to elucidate underlying pathophysiology and maximize development of successful clinical and lifestyle interventions (16-17).

ART technology in endometriosis

The type of ART used depends on factors such as patient age, duration of infertility, and previous treatments (19).

Stimulation protocols: In women selected for IVF, the presence of an endometrioma does not markedly affect responsiveness to hyperstimulation (27).

Simultaneous laparoscopy combined with a modified IVF (GnRH antagonist) protocol may benefit patients with minimal and mild endometriosis.

Traditional GnRH agonist IVF cycles may improve the fecundity rates in women with moderate and severe endometriosis after laparoscopic treatment (40).

Oocyte retrieval: The presence of endometriomas does not generally impair the results of IVF but it increases the risk of infection. There have been several case reports of ovarian abscesses after puncture of endometriomas during ultrasound guided oocyte

retrieval (36,37). A recent case series reported that there remains a significant risk of pelvic abscess even with the prophylactic use of broad spectrum antibiotics (38). Endometriosis can thus raise the risk of pelvic inflammatory disease after oocyte retrieval. More vigorous antibiotic prophylaxis and better vaginal preparation are recommended when oocyte pickup is performed in patients with endometriosis.

Laboratory technology: Endometriosis being a progressive condition, oocyte cryopreservation is being increasingly used by affected young women requiring fertility preservation. Especially in young cases prior to major and complicated surgery for endometriosis, egg banking is offered. From the various techniques available from slow freezing to ultra-rapid freezing, vitrification appears to offer the best outcome.

Overall, while success with IVF for endometriosis may or may not be lower than other infertility diagnoses, the current data suggest that success with IVF for endometriosis is worsened in stage III/IV disease compared to stage I/II disease. Nonetheless, the overall success rate in all stages is good and higher than with expectant management.

- A meta-analysis (Barnhart et al, 2002) on the effects of endometriosis on IVF outcomes concluded that endometriosis interferes with all aspects of the reproductive process and, consequently, success rates among women with endometriosis was almost one half that of patients with other indications for IVF (22). These conclusions, however, are in contrast to the newer registry data from the Society for Assisted Reproductive Technology (SART) 2004–2008 on more than 23,000 assisted reproductive technique cycles with fresh embryo transfers in infertile women with endometriosis compared with all indications for IVF, a total of approximately 450,000 cycles, showing that for all age strata, implantation and live birth rates are similar in women with endometriosis compared with couples with other infertility causes (23, 30).
- Although initial results suggested that fertilization rates were reduced in women with endometriosis compared with those with tubal or unexplained infertility, subsequent larger studies have shown comparable fertilization rates.

- Endometrial receptivity does not seem to be affected as results from egg-donation are not decreased in endometriosis patients.
- Endometriosis, irrespective of its stage, does not affect embryo quality or ART results when ICSI procedure is performed (20, 21, 43).
- Cytokines are key modulators of the immune system and also act as markers of IVF success. Higher follicular Interleukin-23, Interferon-gamma, and Tumour necrosis factor-alpha were found to be associated with endometriosis (44).

Outcomes by severity of disease

- **Mild to severe disease** may be very different entities. Certain defects in folliculogenesis or in the endometrium, might be overcome by the administration of GnRH analogues and controlled ovarian stimulation.
- Associated **deep infiltrating endometriosis** has a negative impact on assisted reproduction results in patients with endometriomas. Moreover, data show that after three IVF-ICSI cycles the clinical pregnancy rate per patient is not improved and that surgery should be considered (41).
- **Stage III-IV** was strongly associated with poor IVF outcome. A decreased fertilization rate in stage I-II might be a cause of subfertility in these women, owing to a hostile environment caused by the disease (45, 46).
- Women with **advanced-stage** endometriosis who have undergone previous surgery respond less well to gonadotropins than women with tubal-factor infertility. However, implantation, pregnancy, and delivery rates are similar, suggesting that embryo quality and uterine receptivity remains unaffected despite diminished ovarian reserve in women with endometriosis (25).
- Patients with endometriosis-associated infertility have pregnancy rates and birth rates similar to tubal factor controls during IVF/ICSI treatment. The exception is women with **endometriomas**, who have lower success rates compared with various stages of peritoneal endometriosis and tubal infertility (21). But also, there are studies that conclude that women with endometriomas achieving pregnancy through IVF do not seem to be exposed to a significant increased risk of obstetrical complications (26).
- Although some early studies suggested that

pregnancy rates following IVF were significantly lower in women with severe endometriosis compared with those with minimal or mild endometriosis (3%/cycle compared with 13%/cycle) (31,32), more recent larger studies have shown no difference in the pregnancy rate following IVF in women with stage 3 or 4 disease compared with stage 1 or 2 disease (30,33,34,35). This may be because of better ovarian stimulation protocols or the transvaginal technique of aspiration of oocytes used in the more recent studies.

Effect of ART on endometriosis

Since endometriosis is an estrogen dependent condition there were concerns expressed regarding the recurrence rates being increased after repeated ovarian hyperstimulation. However, it was concluded by studies that IVF does not expose women to a consistent risk of endometriosis-related symptoms progression (27). It was also found that the cumulative endometriosis recurrence rate is lower after ovarian hyperstimulation for IVF than after lower-dose ovarian stimulation for IUI, suggesting that temporary exposure to very high E(2) levels in women during ovarian hyperstimulation for IVF is not a major risk factor for endometriosis recurrence in women treated with assisted reproductive technology (49, 50).

Conclusion

- Endometriosis associated with infertility is most effectively managed by early aggressive treatment with IVF, with supporting pretreatment wherever it is deemed necessary.
- Different ART are able to bypass most of the endometriosis-related mechanisms of infertility in order to achieve a pregnancy, except for oocyte/embryo quality.
- When considering surgery prior to ART, it is important to weigh the pros and cons of symptom management and pathology-bulk reduction, as against the probable reduction of ovarian reserve.
- If required surgery is to be done then it is noteworthy that the post-surgical reduced ovarian response to hyperstimulation does not translate into poorer IVF outcomes.
- The presence of endometriomas does not generally impair the results of IVF but it

increases the risk of infection.

- Results following IVF in women with endometriosis are comparable to those for women without endometriosis and they do not seem to be significantly affected by the severity of the disease.
- Because a comparable number of embryos are available for transfer, even in patients with advanced disease, the outcome of IVF in terms of implantation and ongoing pregnancy rates are similar in patients with varying severity of the disease.
- The use of GnRH agonists in a long-protocol of ovarian stimulation leads to the highest pregnancy rates, although the role of prolonged pituitary suppression remains unclear.
- In cases of severely compromised ovarian function, egg banking may be offered.

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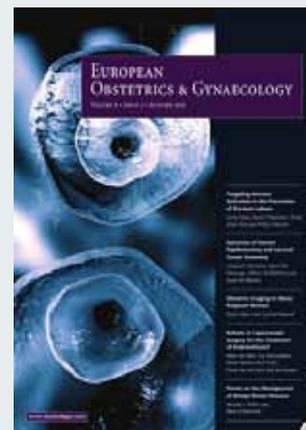
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If WES members wish to receive a hard copy of either of these journals please email **Miriam Oppenheim** at Touchbriefings providing her with your name and postal address.

Letter

Endometriosis-ovarian cancer connection

Dear Editor,

In response to the interesting article on the endometriosis-ovarian cancer connection by Paolo Vercellini, we would like to show the inside of a small endometrioma as seen at transvaginal hydrolaparoscopy. In contrast with other sites of pelvic endometriosis there is abundant superficial endometrium entrapped within the endometrioma, that is in fact a pseudocyst and not a true cyst in the oncologic sense of the word. There are few locations of endometriosis where the ectopic endometrium can develop like within the uterus with a similar hormonal response and bleeding at the time of menstruation.

We agree with the president that the endometrium, neither eutopic in the uterus nor ectopic in the endometrioma, is precancerous. However, it is more likely that at ectopic sites endometrioid cancer arises where more active endometrium is present in abundance. From all ectopic locations this happens to be in the ovary.

We suggest the use of transvaginal access of hydrolaparoscopy for the early proactive detection and (ablative) treatment of even the smallest ovarian endometriomas (figure 1 and 2). They are hardly detectable at transvaginal sonography, in young women in general and infertile women in particular. Image resolution under water is far superior than in an environment of CO² gas for visualisation of filmy adhesions and microvascularisation. Inframillimetric lesions can easily be detected and sampled for pathology (figure 3). At that early stage conservative ablative treatment is far more easy, with distinct cleavage planes and less recurrence.

By extension, the monitoring of patients with a genetically increased risk of ovarian cancer (i.e. with faulty BRCA1, BRCA2 or RAD51D genes) by transvaginal hydrolaparoscopy may well prove to be superior than the present tools, i.e. CA-125, transvaginal sonography or MRI.

Patrick Puttemans and Ivo Brosens

Reference:

Puttemans P, Gordts S, Campo R, Brosens I, Gordts S: 'The transvaginal approach of the small endometrioma in infertile women without obvious pathology: incidence, characteristics, exploration, treatment, recurrence rate and reproductive outcome.' Poster presented at the 11th World Congress on Endometriosis in Montpellier, 04-07/09/2011.



Figure 1



Figure 2



Figure 3

Figure 1 and 2 were taken inside an endometrioma of < 15 mm in diameter

Figure 3 is a close-up of a benign serous surface papilloma of < 0.2 mm in diameter and detected on the surface of the ovary

In memoriam: David Healy

**Professor David Lindsay Healy PhD,
FRANZCOG, FRCOG (Ad Eundem), CREI**

Born on 30 September 1948, Professor David Healy passed away too early on 25 May 2012. He will be dearly missed by the families of his children Ross and Meagan, his brother, sister and his other relatives, his patients, the staff he worked with, and all his colleagues.

Professor Healy graduated from Monash University where he received the Senior Medical Staff prize in 1973. In 1977, he was the first author on a Nature paper, only his third publication as a junior researcher.

In 1979 he completed a PhD at Monash University on Human Prolactin Physiology. David then trained at the Royal Women's Hospital, Melbourne and completed his Obstetrics and Gynaecology specialty training at the National Institutes of Health, USA, and at Edinburgh, Scotland. In 1985, Professor Healy was the first Obstetrician and Gynaecologist to be awarded a Wellcome Trust Senior Clinical Research Fellowship. David Healy became a Professor of the Monash University Department of Obstetrics and Gynaecology in 1990 and its Chairman in 1994. Between 1991 and 1994 he served as the Associate Clinical Dean of the Monash University Faculty of Medicine. He was the Head of the Reproductive Medicine Clinic from 1997. In 2002 Professor Healy became the Chair of the Australian University Departments of Obstetrics & Gynaecology and was awarded an Honorary Fellowship of the Royal College for his many achievements.

One of Professor Healy's great qualities was his unwavering belief in young talent. On the many boards and conference organising committees in which he was involved he would always argue to make room for the new generation. He enjoyed teaching, supervising and mentoring the countless medical students and O&G trainees. Perhaps he also terrified a few in his role as Senior Examiner in Obstetrics and Gynaecology for the



**Professor David Lindsay Healy PhD,
FRANZCOG, FRCOG (Ad Eundem), CREI**

Royal Australian and New Zealand College of Obstetrics and Gynaecology and for the Australian Medical Council. He was also the Director of Education of the Monash IVF Research and Education Foundation.

David also never stopped being an active researcher. He published 255 research articles, wrote 78 book chapters, and edited 8 books, the last one an impressive reference work on endometriosis co-edited by him, Linda Giudice and Hans Evers, *Endometriosis: Science and Practice*. But his academic legacy will certainly live on beyond university libraries. His tremendous passion for high-quality research rubbed off easily on others, and he was a source of enduring inspiration for many impressionable young minds. Students and staff enjoyed his open-door policy and down to earth attitude, and they were often surprised to find a witty raconteur in a relaxed moment.

He served on boards of many learned societies, both nationally and internationally, and was President of the Fertility Society of Australia in 1995. After his term on the board of the Australian Gynaecological Endoscopy Society (AGES), he accepted a position as chairman of the AGES Research Committee and, despite his illness, he continued to play a crucial role on the AGES Education Committee where he helped shape the laparoscopic fellowship syllabus.

While he served on the AGES board, he was also a committed member on the WES board. Bringing the

10th World Congress on Endometriosis to Melbourne in 2008 was a major coup for David. As always, David made sure 'youngsters' like Jim Tsaltas and I got to learn the ropes when he appointed us as scientific programme co-chairs. He was a wonderful mentor and always willing to listen to new ideas. The only thing he would not compromise on was scientific quality and a pre-congress golf tournament for the delegates. His leadership magic turned the WCE2008, hosted by AGES, into a huge success with more than a 1000 delegates.

The accolade he was most proud of was being elected in 2007 as President of the International Federation of Fertility Societies. It was the first time in the 60-year history of the IFFS and that of its sister organisation, FIGO, that an Australian headed either organisation. In an interview he said:

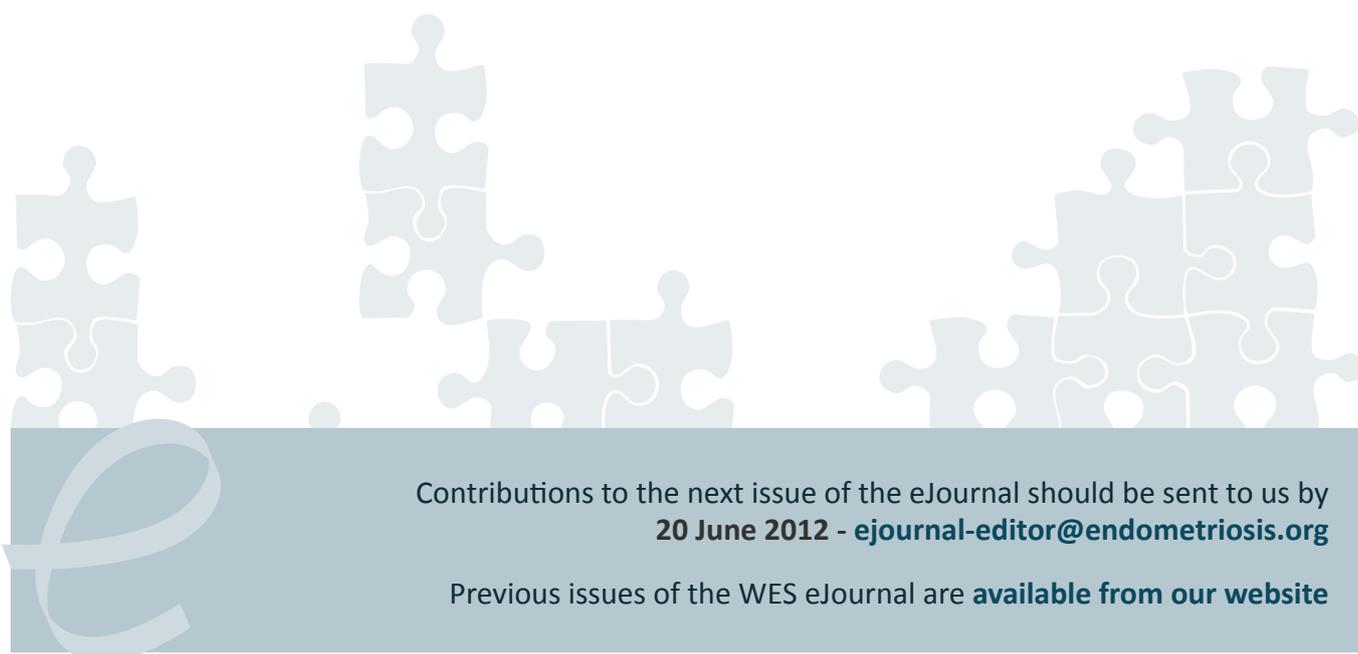
“While in many countries women such as Hillary Clinton exert a strong influence on the political process and can agitate for better health care, IFFS member countries also include those where issues of fertility – especially contraception and abortion – are taboo”.

He had high hopes to bring real change for women in particular from developing countries. He certainly would want us to continue on that path.

Luk Rombauts

A/Professor, Monash University, Australia
eJournal Editor, World Endometriosis Society

You can read additional tributes to Professor Healy on the WES website: <http://endometriosis.ca/news/article/in-memoriam-david-healy/>



Contributions to the next issue of the eJournal should be sent to us by
20 June 2012 - ejournal-editor@endometriosis.org

Previous issues of the WES eJournal are **available from our website**

Your opportunity to help add pieces to the puzzle of endometriosis

Dear Colleagues,

Since 2005 the World Congresses have been largely abstract driven, with very few invited speakers. This successful format provides everyone in the field of endometriosis, regardless of specialty, with the opportunity to have their research presented.

We are now taking this concept one step further by inviting WES members and those who attended WCE2011 to contribute to the selection of topics to which abstracts can be submitted – and ultimately be presented at WCE2014.

This exciting new initiative by the WES Board was announced in the September-November 2011 WES eJournal by our president, Paolo Vercellini, and it is now my pleasure to offer you the opportunity to take part in the voting.

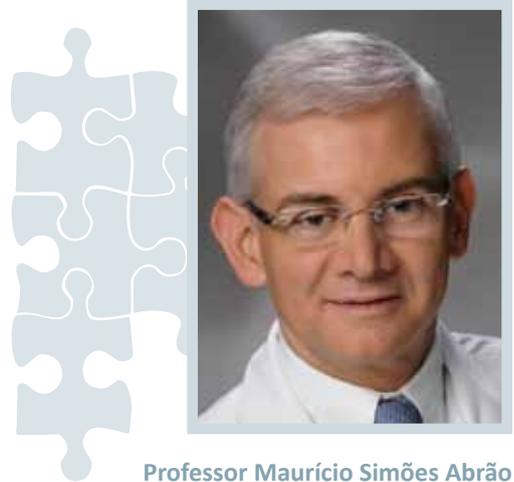
Topics have been collected based on the feedback we received following WCE2011, and you can vote online now: <http://www.surveymonkey.com/s/Q6888J7> You are invited to select the top five topics, which you feel should be in the scientific programme when we all meet again in Sao Paulo in 2014.

The deadline for voting is 20 June 2012, and I'd like to remind you of the words by the WES President: "The world congresses are a success only if we all contribute!"

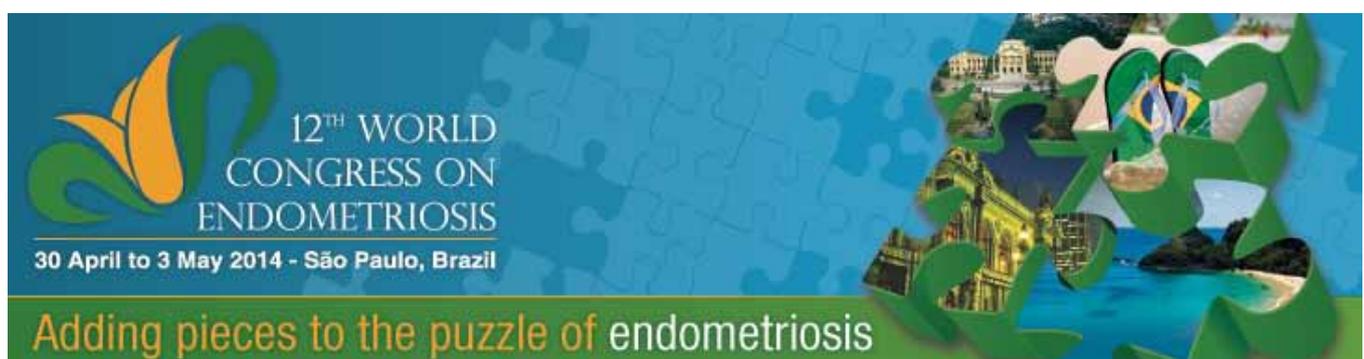
Don't miss out on the opportunity to help add pieces to the puzzle of endometriosis!



Mauricio Simoens Abrao
President
12th World Congress on Endometriosis



Professor Mauricio Simões Abrão
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