



Professor Rodolphe Maboux
President WES

Progress – the operative word!

On the “endometriosis scene” it has been an exciting first quarter. The sheer number of papers, which have been published on endometriosis, is not only remarkable, but is also a strong indicator of how serious the research community is taking this disease, and how much work is going into understanding its pathogenesis and potential future treatment pathways.

As a worldwide Society committed to fostering research in endometriosis, we interpret this as progress. Progress, which we are delighted to be part of – and progress which we wish to continue to encourage and support.

Progress has also been the operative word in Europe, where there has been tremendous achievements through a concerted effort between patient support organisations and physicians working together to make change at legislative level. This has resulted in:

- The Austrian Health Ministry choosing to focus on endometriosis, as one of four diseases to be emphasised during their EU presidency in the first half of 2006; and
- The European Commission making an historic decision to not only include “women’s health” in their 2006 public health work plan, but to include endometriosis in particular!

Successes like these not only recognise that endometriosis needs more focus, but confirm that it is actually getting more focus! I would therefore like to congratulate our European colleagues on the results of their unrelenting lobbying, professionalism, and commitment to pursue legislators to make such important progress happen. This progress benefits us all!

As was highlighted in the January e-journal, the 9th World Congress on Endometriosis was a resounding success. It was yet another step on the ladder of progress. Furthermore, the congress was profitable. This does not mean that the Society is rolling in money, because it is not. However, the financial contribution, which Hans Evers and his team has made possible, will enable us to enhance the services, which we are able to provide to progress in the field of endometriosis – again: it benefits us all! Thus, more congratulations are in order for Hans Evers and his team: they did a great job! They progressed the field of endometriosis!

It is now up to us, as a Society, to build on the progress of the last World Congress – and to progress to the next. We must continue to strive for, encourage, and support research in this field. We must continue to promote national and international information exchange. Let us all contribute to progress this mission. Let us all progress our understanding of endometriosis!

I look forward to continuing working with you all!

Sincerely yours,

Professor Rodolphe Maboux
President, World Endometriosis Society

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Request for collaboration

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Editor's message

Dear colleagues, members of the WES

It is a great pleasure every time I send to each one of you a new issue of the e-journal. In this issue we highlight angiogenesis and endometriosis-related cancer through two interesting papers by Dr Peter Rogers and Dr Edgardo Somigliana. Dr Rogers provides us with an opinion article putting into prominence how angiogenesis is a critical step for endometriosis development, the treatment and the problems related to the potential use of anti-angiogenic agents. Dr Somigliana *et al* provides a review of cohort and case-control studies addressing the potential association between endometriosis and various malignancies and the possible protective effect of oral contraceptives.

I thank the authors for their appreciated contribution and encourage all of you to use the e-journal as a vehicle for sharing thoughts, opinions, collaborative projects, messages, news and articles that may be of interest for our members and help us in our common effort to expand knowledge and to improve endometriosis diagnosis and treatment for the patients' well-being.

Cordially,

Professor Ali Akoum
Editor, WES e-journal

WCE 2008

10 tips to get that airfare

David Healy MD, President WCE 2008

You want to come to Melbourne, Australia for the World Congress on Endometriosis in 2008. Here are ten tips for easing the pain of paying the fare:

1. Piggy bank

Put your coins in a piggy bank. There are 100 weeks until WCE 2008. Your loose change will be about \$10/€10/£7 a week. This provides you with \$1000/€1000/£700 towards the fare!

2. Abstract

Do the research and prepare to submit your abstract for early 2007. The abstract gives you *currency* to approach your department, faculty, university and/or society for funding sources to top up your piggy bank contribution! (Stay tuned to the WES newsletter, and we will give you plenty of warning with registration and program announcements!)

3. Bilateral government cooperative funds

Most governments have these. Give them a call and explore what your government can do for you! Especially after the wonderful news from the European Commission and the Austrian Health Ministry on endometriosis recognition. Your country will have some sort of cooperative to encourage links with Australia, and they will probably have travel support – especially if you can meet them half way (see 1 and 2 above).

4. Pharmaceutical and surgical instrument companies

Meeting our traditional partners half way will always be appreciated (again: see 1 and 2 above).

5. Nett air fares

Take a few moments to compare airfares by e-ticket and in \$AUS. It may be cheaper to buy a ticket from Australia rather than from your own country.

6. Round the world fare

May be cheaper than you think...

7. Two for one fares

Combine your participation in the World Congress with a (probably) much needed break with your favorite traveling companion.

8. Stops enroute

These may lower the air fare and provide an opportunity to see new parts of the world.

9. Group travel

Get your colleagues together, and make this the endometriosis team event of the year!

10. Cake stalls, sausage sizzlers, and the odd marathon

If all else fails, get cooking or get running...!



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Don't miss our priceless article on [how to get over jetlag](#), featured in the January 2006 WES e-journal.

GUEST EDITORIAL

Angiogenesis and endometriosis

Associate Professor Peter A W Rogers

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There have been a number of recent scientific publications either theorising that it should be possible to reduce the impact of endometriosis by inhibiting the growth of new blood vessels supporting the endometriotic lesion, or presenting data from animal models showing that angiogenesis inhibitors can inhibit the growth of endometriotic explants. To further explore the potential utility of angiogenesis inhibitors in treating endometriosis, it is important to have some understanding of the complexities of angiogenesis as a biological process.

Angiogenesis is defined as the process whereby new blood vessels are formed from pre-existing vessels. Depending on their metabolic activity, any cluster of cells greater than approximately 1mm³ cannot receive sufficient oxygen or nutrients by diffusion alone, and hence requires supply by functioning blood vessels. There are at least 4 different mechanisms by which angiogenesis can occur: sprouting, intussusception, elongation/widening, and incorporation of circulating endothelial cells into vessels (Folkman and D'Amore, 1996, Risau, 1997, Asahara *et al*, 1999, Burri and Djonov, 2002). Each mechanism involves a different series of steps that can include activation of endothelial cells, breakdown of the basement membrane, migration and proliferation of endothelial cells, tube formation, and stabilisation of the tube with the formation of new basement membrane and coverage of the vessel wall with pericytes and vascular smooth muscle cells.

To add to the complexity of multiple mechanisms and steps of angiogenesis, numerous factors have been identified as playing direct or indirect roles in regulating each part of the angiogenic process. In human endometrium, where the angiogenic mechanisms are potentially similar to those in endometriotic lesions, blood vessels grow and regress every menstrual cycle under the overall control of oestrogen and progesterone. However, regulation of endometrial angiogenesis is not simple, with evidence now emerging that oestrogen can both promote and inhibit endometrial vessel growth under different circumstances (Girling and Rogers, 2005). In addition, a large number of angiogenic factors and inhibitors have been identified in human endometrium, although the precise role they play in regulating angiogenesis during the menstrual cycle and pregnancy remains to be elucidated.

The many regulatory factors and steps contributing to each angiogenic mechanism provide a large number of different targets for disruption or inhibition. As a consequence, many naturally occurring and synthetic compounds with anti-angiogenic activity have now been identified. While all of these have demonstrable anti-angiogenic activity in *in vitro* or defined *in vivo* models, it is a common observation

that their ability to completely block angiogenesis *in vivo* is often restricted. An explanation for this observation may be that since angiogenesis is such a fundamental process for survival of the organism, alternative pathways rapidly come in to play if one step is blocked. Examples of alternative pathways, or redundancy, can be found in other biological processes that are fundamental to evolutionary survival.

In assessing the potential of anti-angiogenic therapy as a treatment for endometriosis, it is relevant to consider 2 major issues: the likely effectiveness of the treatment, and the risk of unwanted side effects.

The potential effectiveness of anti-angiogenic therapy for treating endometriosis can only be assessed based on limited animal studies, since to date there have not been any reported clinical trials in humans. One of the initial animal studies used human endometrial tissues transplanted to immunocompromised nude mice, and inhibited angiogenesis through limiting availability of vascular endothelial growth factor (VEGF) by using either a truncated soluble receptor, or a purified VEGF antibody (Hull *et al*, 2003). Both reagents significantly inhibited endometrial explant growth within the mice, with pericyte-free vessels being significantly reduced. The same authors also reported that a large number of blood vessels supplying endometriotic lesions in women are devoid of pericytes, and hence in theory should also be vulnerable to disruption by anti-angiogenic agents. A second study, using a similar human endometrial tissue into nude mouse transplantation model, investigated 4 different anti-angiogenic agents, administered 3 weeks after the endometrial explants had been transplanted (Nap *et al*, 2004). All 4 inhibitors were able to reduce established explants, with the pericyte free vessels again being targeted. This study also reported that angiogenesis associated with other events such as wound healing and uterine growth were unaffected by the treatments, although this was not investigated in great detail. An alternative experimental model uses endometrium surgically removed from and transplanted back into the same animal. In hamsters, growth of such autologous endometrium transplanted into a dorsal skinfold chamber can be more effectively blocked by compounds that inhibit a number of angiogenesis factors simultaneously (VEGF, fibroblast growth factor and platelet derived growth factor), rather than VEGF alone (Laschke *et al*, 2006).

There is always a concern with anti-angiogenic therapy that blood vessel growth necessary for normal function may be blocked. In a model using mouse endometrium transplanted into mouse peritoneal cavity, Dabrosin *et al* (2002) reported that overexpression of the angiogenic inhibitor angiostatin by adenoviral transfection eradicated established endometrial explants, but also impaired ovarian function, decreased

uterine weight and increased body weight. Significant angiogenesis occurs in the female reproductive tract during the ovulatory cycle, with the ovarian follicle, the corpus luteum and the uterine endometrium all exhibiting active angiogenesis. Unwanted inhibition of angiogenesis in these organs would be a significant problem. In other studies where side effects of anti-angiogenic therapy were monitored, it has been reported that endostatin, and a short peptide derived from endostatin, are able to inhibit endometrial transplants in mice by approximately 50% without affecting angiogenesis in other organs (Becker *et al*, 2005, 2006).

These experiments raise a number of issues. All rely on transplantation of existing normal endometrium into the peritoneal cavity, rather than spontaneous growth of endometriotic lesions as occurs in humans. It is unclear whether the specific angiogenic mechanisms being studied in the endometrial transplant animal models are the same as those that occur in the different spontaneous types and stages of human endometriotic lesions. The animal experiments are all short-term, while endometriosis is a chronic disease where treatment may need to be given over years. Thus, by the time symptoms occur and a diagnosis is

reached in humans, the most suitable time for angiogenesis inhibitor treatment may be well past. Finally, and of greatest concern, is the risk of giving angiogenesis inhibitors to women who may be pregnant. Angiogenesis is an essential component of normal growth and development of the foetus, and any inhibition of normal vessel growth can have dire consequences for the unborn child, as experience with thalidomide tragically demonstrated.

So where to from here? Clearly, more basic knowledge is required about both the pathophysiology of endometriosis, and the mechanisms of angiogenesis and how to inhibit them. It is possible that endometriosis-specific angiogenic mechanisms could be identified and safely targeted, thus allowing long-term treatment without risk of unwanted side effects. Alternatively, very specific short-term treatment regimens could be devised to reduce endometriotic burden prior to specific events such as surgery. Realistically, and regardless of the science, it is questionable in the modern litigious age whether in the light of past history any company would be prepared to take the risk of marketing anti-angiogenic pharmaceuticals to women who might become pregnant while using them.

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REVIEW ARTICLE

A literature review of clinical and epidemiological studies addressing the risk of cancer in endometriosis

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Introduction

In the last decade endometriosis has been associated with a definite increase in risk of various malignancies (1). In order to assess the entity and the nature of this association, we have critically evaluated observational, cohort and case-control studies performed on this topic with a specific focus on their problems and limitations (1).

Evidence from clinical series

Based on Sampson's (2) and Scott's (3) criteria to identify malignant tumors raised from endometriosis, few groups have evaluated the prevalence of ovarian malignancy in large series of patients operated for endometriosis. A prevalence of about 0.9% has been observed. Unfortunately, all currently available series are retrospective, and thus probably unable to properly address this point. In support to this idea, the same prevalence differed significantly according to the pathologists who performed the analysis.

A prospective, sufficiently large and unbiased series evaluating the frequency of ovarian cancer concomitant to endometriosis is currently not available.

Whether or not endometriosis should be considered a preneoplastic disease represents a major and controversial issue. Studies on the epithelial lining of cystic ovarian endometriosis have documented the presence of metaplastic, hyperplastic or atypical changes whose prevalence in endometriosis is not defined (revised in Somigliana et al, 2006) (1). Data on metaplasia are scanty and controversial. Differences among the studies may be due, at least in part, to a different study population and/or to selection biases. Moreover, the presence of neoplasm *per se* might induce metaplasia in the adjacent endometriosis. Overall, there is insufficient evidence supporting metaplasia of endometriotic lesions as a preneoplastic condition. Data on atypia are more univocal and document a highly significant increased presence of severe atypia in endometriotic lesions in patients

Table I. Studies on the frequency of endometriosis in patients with ovarian cancers according to the malignant histotype.

Authors	Ovarian cancer histotype					Total
	Serous	Mucinous	Endometrioid	Clear cell	Other	
Aure <i>et al.</i> , 1971	0% (0/357)	1% (1/203)	9% (20/212)	24% (14/59)	...	4% (35/831)
Kurman <i>et al.</i> , 1972	6% (7/118)	4% (2/47)	11% (4/37)	8% (2/28)	...	7% (15/230)
Russel, 1979	3% (7/233)	4% (3/69)	28% (20/72)	48% (16/33)	...	11% (46/407)
Vercellini <i>et al.</i> , 1993	4% (8/220)	6% (6/94)	26% (30/114)	21% (8/38)	12% (11/88)	11% (63/556)
De La Cuesta <i>et al.</i> , 1996 ^a	0% (0/10)	6% (1/18)	39% (9/23)	41% (7/17)	45% (5/11)	28% (22/79)
Toki <i>et al.</i> , 1996	10% (9/88)	9% (3/33)	30% (16/54)	50% (22/44)	0% (0/16)	21% (50/235)
Jimbo <i>et al.</i> , 1997	9% (8/92)	3% (1/35)	23% (3/13)	41% (13/32)	...	15% (25/172)
Fukunaga <i>et al.</i> , 1997	10% (6/63)	6% (2/35)	42% (13/31)	54% (27/50)	67% (2/3)	27% (50/182)
Ogawa <i>et al.</i> , 2000	7% (4/60)	0% (0/17)	43% (3/7)	70% (30/43)	...	29% (37/127)
Vercellini <i>et al.</i> , 2000	3% (2/61)	3% (1/30)	20% (13/66)	14% (5/35)	6% (1/17)	10% (22/209)
Oral <i>et al.</i> , 2003	4% (3/70)	6% (2/35)	22% (4/18)	9% (1/11)	8% (4/49)	8% (14/183)

Those studies evaluating association with at least endometrioid, clear cell and seromucinous histotypes have been included.

^a Only Stage I cancers were included.

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Association between endometriosis and cancer: A comprehensive review and a critical analysis of clinical and epidemiological evidence. *Gynecol Oncol* 2006.

with endometriosis-associated ovarian cancer when compared to patients with endometriosis alone. Finally, data on endometriotic hyperplasia, although very limited, also support a possible association with the malignant transformation. These data suggest that carcinoma may arise from endometriosis through a multi-step phenomenon where typical endometriosis may change into severe atypia with or without hyperplasia and then into carcinoma. Nevertheless, conclusive evidence supporting this model is lacking. Studies prospectively evaluating the risk of cancer in patients with endometriotic atypia and/or complex hyperplasia are extremely scarce and inconclusive. A major limit in investigating the potential malignant transformation of these lesions is that during a surgical intervention for endometriosis, excision of endometriomas is generally complete and, consequently, it may be argued that atypical lesions are practically absent after surgery.

A 4-29% frequency of endometriosis was found in cases operated for ovarian tumors (Table I). These percentages do not appear to be very different from the 10% supposed prevalence of the disease in the reproductive age. On the other hand, a consistent body of evidence has documented a clear association between endometriosis and endometrioid and/or clear cell ovarian carcinomas (Table I). This observation represents one of the most important issues supporting a possible causal relationship between endometriosis and ovarian cancer.

In regard to the clinical behaviour and prognostic factors in ovarian cancer patients with or without concomitant

endometriosis, patients affected tended to be younger and to be diagnosed in earlier stages and with lower grade lesions (4-8). A better prognosis could be demonstrated in these patients. It remains to be clarified whether the less frequent dissemination outside the ovaries in cancers arising from endometriosis may be due to a different pathological behaviour of the malignancy *per se* or whether it may be related to the destruction of endometriotic lesions in more advanced cancers. Furthermore, a diagnostic bias could also explain, at least in part, the increased diagnosis in initial stages. The typical symptoms of endometriosis might facilitate earlier diagnosis.

Endometriosis and ovarian cancer: evidence from population-based studies

Data from the majority of the available cohort and case-control studies tend to suggest an association between endometriosis and ovarian cancer, although it is difficult to precisely estimate the effect size as the observed increase in risk ranges from 30 to 90% (Table II) (revised in Somigliana et al, 2006) (1). In epidemiology, a relative risk of less than two is considered to indicate a weak association and weak associations are more likely to be explained by unrelated biases. Some limitations of available studies have to be considered:

1. confounders have not always been controlled adequately. It is well known that parity and oral contraceptive use represent strong preventive factors and measures of association should at least be controlled for these two factors. It cannot be ruled out that some medical

Table II. Relationship between endometriosis and ovarian cancer

Studies	Study design	Entity of the association	
		OR, SIR or RR	95% CI
Brinton <i>et al.</i> , 1997 ^a	Cohort	1.9	1.3-2.8
Ness <i>et al.</i> , 2000	Case-control	1.7	1.2-2.4
Ness <i>et al.</i> , 2002	Case-control	1.7	1.1-2.7
Brinton <i>et al.</i> , 2004	Cohort	1.3	0.6-2.6
Borgfeldt and Andolf, 2004	Case-control	1.3	1.0-1.7
Modugno <i>et al.</i> , 2004	Case-control	1.3	1.1-1.6
Brinton <i>et al.</i> , 2005	Cohort	1.7	1.3-2.1
Melin <i>et al.</i> , 2006	Cohort	1.4	1.2-1.7

OR: Odds Ratio, SIR: Standardized Incidence Ratio, RR; Relative Risk.
CI: Confidence Interval.

^a The study from Melin *et al.* (2006) is an extension of the study from Brinton *et al.* (1997).

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Table III. Relationship between endometriosis and non-ovarian gynaecological cancers.

Studies	Study design	Entity of the association	
		OR, SIR or RR	95% CI
Breast cancer			
Moseson <i>et al.</i> , 1993	Case-control	4.3	0.9-20.4
Schairer <i>et al.</i> , 1997 (A)	Cohort	3.2	1.2-8.0
Schairer <i>et al.</i> , 1997 (B)	Cohort	3.0	0.7-4.1
Brinton <i>et al.</i> , 1997	Cohort	1.3	1.1-1.4
Weiss <i>et al.</i> , 1999	Case-control	1.1	0.7-1.8
Venn <i>et al.</i> , 1999	Cohort	1.0	0.7-1.5
Olson <i>et al.</i> , 2002	Cohort	1.0	0.8-1.2
Borgfeldt and Andolf, 2004	Case-control	1.1	1.0-1.2
Brinton <i>et al.</i> , 2005	Cohort	0.8	0.6-1.1
Cervical cancer			
Brinton <i>et al.</i> , 1997 ^a	Cohort	0.7	0.4-1.3
Berglund <i>et al.</i> , 2003 ^a	Cohort	0.6	0.5-0.8
Borgfeldt and Andolf, 2004	Case-control	0.6	0.4-0.9
Endometrial cancer			
Brinton <i>et al.</i> , 1997	Cohort	1.1	0.6-1.9
Olson <i>et al.</i> , 2002	Cohort	1.2	0.6-2.5
Borgfeldt and Andolf, 2004	Case-control	0.6	0.4-0.8
Brinton <i>et al.</i> , 2005	Cohort	0.8	0.3-1.9
Melanoma			
Wyshak <i>et al.</i> , 1989	Case-control	3.9	1.2-12.4
Frish and Wyshak, 1992	Case-control	1.1	0.5-2.3
Holly <i>et al.</i> , 1995	Case-control	0.9	0.5-1.4
Brinton <i>et al.</i> , 1997	Cohort	1.0	0.7-1.5
Olson <i>et al.</i> , 2002	Cohort	0.7	0.2-1.8
Brinton <i>et al.</i> , 2005	Cohort	2.1	1.0-4.4
Non-Hodgkin's lymphoma			
Brinton <i>et al.</i> , 1997 ^a	Cohort	1.8	1.2-2.6
Olson <i>et al.</i> , 2002	Cohort	1.7	1.0-2.9
Berglund <i>et al.</i> , 2003 ^a	Cohort	1.2	1.0-1.5

OR: Odds Ratio, SIR: Standardized Incidence Ratio, RR; Relative Risk, CI: Confidence Interval.

The study from Schairer *et al* focused on two different cohorts: patients who underwent hysterectomy (A) and those who underwent oophorectomy (B).

^a The study from Berglund *et al* (2003) is an extension of the study from Brinton *et al.*(1997).

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- treatment options of endometriosis may also influence the hazard of ovarian cancer;
2. studies assume that the identification of endometriotic lesions during a surgical intervention corresponds to the presence of the disease in that particular patient. However, surgery is aimed to eradicate the disease. Since recurrence of endometriosis is not a systematic occurrence, the assumption that all operated patients remain affected may lead to an underestimation of the risk;
 3. the generalisation of the results to all women with endometriosis might be incorrect, as most of the observations refer to women affected by advanced forms necessitating hospitalisation and surgery;
 4. insights from clinical series indicate that endometriosis is linked only to endometrioid and clear cell ovarian carcinomas and not to other malignant histotypes (Table I). These histologic diagnoses represent about one third of all epithelial ovarian cancers. Unfortunately, most epidemiologic studies focus on ovarian cancer in general. This may have attenuated the entity of the observed associations. Studies specifically considering these two histotypes suggest an increased association but number of observed cases are extremely low (9, 10).

Hence, some limitations may have biased results towards the null hypothesis whereas others may have led to overestimate the association.

Endometriosis and other cancers

The potential association between endometriosis and breast cancer remains unclear should be interpreted with caution, because of the small number of subjects reporting the condition, the trend towards a protective effect in postmenopausal women observed in some studies and the lack of consistency among studies (Table III) (revised in Somigliana et al, 2006) (1). The documentation of a reduced risk of cervical cancer in patients with endometriosis using the National Swedish Cancer Register is unexpected (Table III) and could be interpreted in terms of increased number of referrals to a gynaecologist from patients with endometriosis. An association between melanoma and endometriosis has been repeatedly reported by a single research group (Table III). In general, these studies collected a limited number of subjects, concerned dysplastic nevi, a well-known precursor of melanoma, rather than the cancer itself and were characterized by too many sub-analyses in relation to the casistics evaluated. Results from large independent observational studies are controversial in this regard (Table III). A statistically significant increased risk of melanoma in the order of two-fold was documented in infertile women with endometriosis when compared to patients with other causes of infertility in a recent study by Brinton *et al* (11).

The two largest population-based cohort studies have independently documented the association between non-Hodgkin's lymphoma and endometriosis (Table III). However, the statistically significant results from these studies

are based on a small number of observed cases and need further confirmation.

Discussion

Current evidence is robust enough to sustain a link between endometriosis and ovarian cancer. However, the demonstration of an association between two conditions cannot be used to infer causality. Two possible scenarios may be envisioned to explain this link:

1. Endometriotic cells might undergo somatic mutational events able to confer to the cells the malignant potential characteristics of cancer. Endometriosis would be the precursor of some, if not all, ovarian cancers of endometrioid and clear cell histologic types. Support to the idea of the ectopic tissue as the benign precursor of some ovarian cancers comes from those cases of evident histologically-proven transition from the benign disease to the malignant entity.
2. Alternatively, endometriosis and ovarian carcinoma might represent two distinct biological entities characterised by a different set of causative molecular events and their relative frequent coexistence may derive from the sharing of some risk factors or antecedent mechanisms. Nulliparity and menstrual characteristics are well known determinants of the risk for both the conditions.

At present, we are unable to disentangle this issue; the idea that, in rare cases, the ectopic tissue undergoes malignant transformation cannot be refuted but we are unable to quantify the entity of this process and consequently to infer that causality should be advocated to explain the increased risk of specific histotypes of ovarian cancer in women with endometriosis. Consequently, from a clinical point of view, it is questionable whether a systematic and serial surgery may be justifiable in women with endometriosis based on the assumption that eradication of visible lesions would abolish this increase in risk. On the other hand, it is well known that oral contraceptives have a protective effect of on ovarian cancer risk in general. Oral contraceptive use is associated with a substantial and duration-dependent reduction in risk, with an observed 80% lower occurrence of ovarian cancer in women with endometriosis who use the drug for >10 years (12). This approach seems preferable to the uncertain results of a repetitive surgery that, in these patients, is sometimes associated with major morbidity due to severely distorted anatomical conditions.

For other types of tumours, no modifications in the standard, age-related diagnostic evaluations for the early detection of cancer are suggested. Women with endometriosis should undergo the usual dermatologic surveillance suggested for the general population. General practitioners and gynaecologists should be aware of the possibility that women with endometriosis are at increased risk of non-Hodgkin's lymphomas, and consequently, should seek prompt evaluation in case of recurrent infections, unexplained fever, persistent cough, or weight loss but due to the small number of patients that develop non-Hodgkin's lymphoma in the general population, no major invasive diagnostic investigations seem warranted in women with endometriosis undergoing routine screening programs.

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Upcoming meetings

World Meeting on Gynaecological Pelvic Pain and Endometriosis

10 - 14 May, 2006
Milano, Italy
www.milan2006.it

AGES 2006: Managing common gynaecological challenges

4 - 6 May 2006
Adelaide, Australia
www.ages.com.au/events.htm

ESHRE pre-congress course by the Special Interest Group on Endometriosis: IMPLANTATION

18 June 2006
Prague, Czech Republic
www.eshre.com/emc.asp?pageId=307

2nd Nordic Congress on Endometriosis

25 - 27 August 2006
Svendborg, Denmark
www.nce06.com

VIIth PAX meeting

28 - 30 September 2006
Leuven, Belgium
www.gynsurgery.org/pax/index.html

IFFS 19th World Congress on Fertility and Sterility

29 April - 3 May 2007
Durban, South Africa
<http://www.iffs2007.org.za/>

For a full congress schedule please see www.endometriosis.org/congress.html

CONGRESS SCENE

Highlights from Endometriose 2006 (23 – 25 March 2006, Sao Paulo, Brazil)

Professor Mauricio Abrao, University of Sao Paulo and Professor Carlos Petta, University of Campinas, Brazil

The Endometriosis 2006 symposium, which attracted 340 participants, focused on the new aspects of the etiopathogenesis of the disease, diagnosis, infertility, surgical, and medical treatment. It also addressed the impact of the disease, as well as guidelines for the diagnosis and management of endometriosis. Uniquely to this meeting, however, was the assessment of the *impact* of the lectures at the end of the three days, resulting in “take home messages” for the individual clinician and the conclusion that evidence based medical education can change clinical practice and thus ensure the best interest of the patients.

Main aspects

The opening lecture, “The patient as a partner”, set the scene for the importance of multi-disciplinary collaboration in dealing with the challenges of endometriosis, and for making progress at legislative level as has recently been demonstrated with the European Commission. It was delivered by Lone Hummelshøj (UK) who, together with Professor Charles Chapron (France), also presented on the development and use of the [ESHRE guideline for the diagnosis and treatment of endometriosis](#). Professor Chapron also discussed his experience with the surgical treatment of deeply infiltrating endometriosis and presented results of trans-rectal ultrasound. Ultrasound may be the first option of image evaluation for deeply infiltrating endometriosis, and which in experienced hands can give a precise evaluation of lesions.

Harry Reich (USA) talked about hysterectomy and endometriosis and the evolution of the surgical treatment over the last three decades. He demonstrated that nowadays laparoscopic surgery is the main treatment for advanced disease. Peter Maher (Australia) presented lectures on colorectal surgery and the overall complications of surgical treatment, concluding how important it is to make proper decisions about surgical treatments in order to avoid complications.

During the meeting it became apparent that the intense research activity developed in Brazil contributed to a highly interactive meeting, which included: epidemiology, genetics, immunology, diagnosis and treatment of the disease. Recent studies about genetics, ambient factors, imaging diagnosis, treatment of infertile patients as the association between endometriosis and cancer were presented.

Assessing the impact of attending a congress

As a unique component, we decided to assess on the last day if the messages delivered by our key note speakers had had any influence on the way in which the delegates would go back and continue their clinical practice.



*Congress organisers
Mauricio Abrao and Carlos Petta*

Prior to the congress, the website www.endometriose2006.net had posed seven questions regarding various aspects of the clinical management of endometriosis, and had gathered opinions from more than 200 gynaecologists, radiologists colorectal surgeons, and urologists.

On the last day of the congress, we carried out the “Brazilian Consensus on the Diagnosis and Treatment of Endometriosis”, where Brazilian participants voted again in an interactive session on how to deal with:

- diagnosis
- treatment of pain
- infertility
- ovarian disease
- deeply infiltrating endometriosis.

The original answers (pre-congress) were then compared to the results obtained at the end of the meeting. And there was a difference! In dealing with ovarian disease the most frequent answer before the meeting was to aspirate the ovarian endometrioma, whereas after the meeting, where the evidence of the ESHRE guideline had been presented, the most frequent answer was to remove the capsule of the ovarian endometrioma.

Analysing the clinical treatment, physicians re-evaluated the indications of the use of GnRH-analogues, following an interactive discussion at the meeting. The question, which had been asked was:

CASE STUDY: infertile patient of 34 years with severe pain and deep endometriosis compromising the rectum. Imaging methods show the lesion compromising the layers serosa, muscularis and submucosa. The investigation of the male factor was normal.

What would you recommend?

48.3% (before the meeting) and 11.9% (at the end of the meeting) of our colleagues answered that three months of GnRH-analogues would be indicated and after this period, the patient should be submitted for laparoscopic surgery. 33.3% (before the meeting) and 52.4% (at the end of the meeting) of our colleagues answered that surgical treatment of the bowel disease would be the best treatment.

In summary, after the meeting the indication of preoperative treatment with GnRH-analogues for bowel endometriosis decreased and the indication for surgical treatment in patients with severe pain increased.

Conclusion

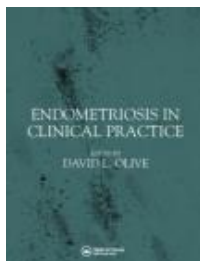
The aim of Endometriose2006 was to provide state of the art presentations on one topic (in this case: endometriosis) in a “one-room” scenario (ie. no parallel/competing sessions) to enable discussion and to aid clinicians to

contribute with feedback/experience of their day-to-day practice.

We succeeded by ensuring that the key messages, based on the latest available evidence, were delivered by national and international specialists in endometriosis in a way that could be effectively applied in clinical practice.

In evaluating the “take-home-message”, both before and after the congress, by asking for feedback on “seven issues”, we proved that from an educational point of view well presented up-to-date clinical evidence can aid in, and potentially change, clinical practice. This becomes increasingly important with the development of new tools for pre-operative diagnosis of the disease, to ensure that the best decisions about individual treatments for the patients are chosen. Educational meetings such as these can aid in ensuring that ongoing emphasis is placed on evidence based medicine and the clinical application of this.

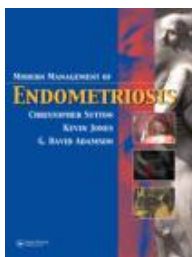
Books on endometriosis



Endometriosis in clinical practise

edited by David Olive

This colour illustrated project brings together 37 international experts to demonstrate what is known about endometriosis and the clinical implications for the woman suffering from the disease. The contributors work their way through the pathogenesis of endometriosis, its theories and the underlying biology, symptoms, diagnosis, health status of women with the disease, through to current clinical treatment options.



Modern management of endometriosis

edited by Christopher Sutton, Kevin Jones and G David Adamson

This book, written by an internationally recognised team of experts, covers the full range of surgical and medical interventions for diagnosing and treating endometriosis. It will help gynaecologists refine their operative technique and consider new approaches to this highly challenging disease.



Surgical management of endometriosis

edited by David Redwine MD

This illustrated monograph brings together respected authorities on the surgical management of endometriosis. The editor has been closely associated with the development of many of the laparoscopic techniques used around the world for the surgical management of endometriosis.

Research highlights

Small nerve fibres detected in the functional layer in all women with endometriosis may have important implications for understanding the generation of pain in these patients. The presence of nerve fibres in an endometrial biopsy may be a novel surrogate marker of clinical endometriosis.

[Tokushige N, Markham R, Russell P, Fraser IS. High density of small nerve fibres in the functional layer of the endometrium in women with endometriosis. Human Reprod 2006; 21\(3\): 782-787.](#)

A Cochrane review has found that endometriosis patients who use gonadotropin-releasing hormone (GnRH) agonists in the run-up to IVF have improved outcomes.

[Sallam HN, Garcia-Velasco JA, Dias S, Arici A. Long-term pituitary down-regulation before in vitro fertilization \(IVF\) for women with endometriosis. Cochrane Database of Systematic Reviews 2006; 1.](#)

The proliferative activity of early ovarian clear cell adenocarcinoma seems to depend on the association of this cancer with endometriosis. When endometriosis is associated with ovarian clear cell adenocarcinoma, there is a change of its cytokine production that may inhibit tumour growth.

[Komiyama SI, Aoki D, Katsuki Y, Nozawa S. Proliferative activity of early ovarian clear cell adenocarcinoma depends on association with endometriosis. Eur J Obstet Gynecol Reprod Biol 2006.](#)

Expression of class I human leukocyte antigen (HLA D) is significantly higher in endometrial samples from patients with endometriosis than in those from other people.

[Vernet-Tomas del M, Perez-Ares CT, Verdu N, Molinero JL, Fernandez-Figueras MT, Carreras R. The endometria of patients with endometriosis show higher expression of class I human leukocyte antigen than the endometria of healthy women. Fertility and Sterility 2006; 85: 78-83.](#)

Women with a specific type of uterine anomaly appear to be at high risk of endometriosis, even though their menstrual flow is not obstructed, researchers report.

[Nawroth F, Nawroth F, Rahimi G, Nawroth C, Foth D, Ludwig M, Schmidt T. Is there an association between septate uterus and endometriosis? Hum Reprod. 2006; 21\(2\): 542-4.](#)

A low-dose norethindrone acetate could be considered an effective, tolerable, and inexpensive first-choice medical alternative to repeat surgery for treating symptomatic rectovaginal endometriotic lesions in patients who do not seek conception.

[Vercellini P, Pietropaolo G, De Giorgi O, Pasin R, Chiodini A, Crosignani PG. Treatment of symptomatic rectovaginal endometriosis with an estrogen-progestogen combination versus low-dose norethindrone acetate. Fertil Steril 2005; 84\(5\):1375-87.](#)

Request for collaboration: adenomyosis uteri

Dr Victoria Pechenikova from St Petersburg, Russia, specialises in pathomorphology and obstetrics and gynecology. She has been working as a researcher since 1996, and is interested in the problem of adenomyosis uteri. Her scientific work includes: adenomyosis cancerous transformation, adenomyosis morphofunctional characteristics, adenomyosis and leiomyoma concomitance, adenomyosis and perifocal leiomyocyte hyperplasia.

Dr Pechenikova has a great deal of data of patients who have had surgery for adenomyosis, and is interested in its pathogenesis. She would like to get in contact with other doctors/scientists, who are interested in collaboration and the exchange of scientific information. She speaks Russian, English and Italian.

Contact Dr Victoria Pechenikova at v_pechenikova@hotmail.com