eJOURNAL

July / August 2010

THE PRESIDENT's MESSAGE

Endometriosis is the right disease – right now!

Professor Hans Evers
WES President

With this statement the famous actress Whoopi Goldberg called upon the attendants at last year's inaugural Endometriosis Blossom Ball in New York City to raise awareness of endometriosis and sponsor research.

Ms Goldberg is a role model. A role model is a famous public personality who serves as an inspiring example, and whose positive behaviour is copied by others.

It is difficult to overestimate the effect of role models. Due to people like Padma Lakshmi, Emmy-award nominee and famous US TV-chef, the Massachusetts Institute of Technology was able to launch its new Center for Gynepathology Research for the study of endometriosis earlier this year.

"The new centre will provide scientists, clinicians and engineers with fantastic opportunities to study the basic biology behind the disease, and its diagnosis, prevention and treatment" commented Keith Isaacson, Scientific Co-Director of the Centre.

At this year's Blossom Ball, the Endometriosis Foundation of America (EFA) honoured Dr Linda Griffith from the MIT with an award for her longstanding commitment to the science and treatment of endometriosis. In her acceptance speech Dr Griffith stated: "*I have lots of things I do at NIH and everywhere else and I was always too busy to do anything substantial for endometriosis. I read this article … and I then immediately e-mailed my lab and said, okay, so… I do not watch TV. I said who is Padma Lakshmi and people wrote me back instantly. I said we have her up here to help launch this center and there is like … oh my God! You are going to have Padma Lakshmi come to MIT! There was this amazing response from students … and I was actually kind of nervous. I have never had a celebrity … and Padma came … and she was incredible …*". This shows you the effect of role models: even celebrated scientists get weak at the knees. But subsequently the support for investigating the disease at MIT has increased tremendously!

It is quite obvious that if this can be achieved by involving role models in our campaign to fight endometriosis we need more famous people with endometriosis like Whoopi Goldberg, Padma Lakshmi, Marilyn Monroe, Diana Wallis and perhaps Hillary Clinton (thank you Google!) to speak up and join us in convincing sponsors and secure funding for much needed research into preventing this disease in future generations. After all, more young women are suffering from endometriosis than from any other disease.

That the vast majority of these women suffer in silence, most even unaware of the cause of their suffering, doesn't mean to say that they do not deserve support. They do. And we need and must provide this support.

Endometriosis is the right disease, right now!





In this issue of the WES e-Journal

President's message	1
A word from the editor	2
Upcoming meetings	2
Guest editors' research digest	3
Announcements	7
WCE2011 update	8

ISSN 1993-3924

World Endometriosis Society

Central Business Office
89 Southgate Road
London N1 3JS
England
t +44 (0)77 1006 5164
www.endometriosis.ca
wes@endometriosis.org

© 2010 World Endometriosis Society

A WORD FROM THE EDITOR

Do celebrities have endometriosis too?

Dr Luk Rombauts
WES e-Journal Editor

All right, you are all too late and I feel let down. In the last edition I made it clear that I was desperate for some good advice. The socceroos were looking for a replacement for Pim Verbeek, the Netherlands-born coach who led the socceroos to their third-ever world cup campaign. He received credit for that achievement, but the Australian media didn't spare him after he chose not to field any recognised strikers in their opening match against Germany, which they lost 0-4.

So now, it's been decided. We have a German coach: Holger Osieck, previously the wingman of the famous Franz Beckenbauer when he took the 'Mannschaft' to their cup win in 1990. You would hope that his inside knowledge will give us a better fighting chance against the Germans when we meet them next time. But enough about football!

Our president Hans Evers introduces this issue with his musings about stardom, role models and raising awareness. Given the prevalence of this condition, I wonder which other celebrities have been suffering in silence for too long? Perhaps the catch cry should be: **'Endometriosis is the right disease *to come out with*, right now'**. We desperately need all of them to help raise more research funding: there is no lack of ideas and research proposals – funding is our eternal challenge!

In this edition, our guest editors Aimee Browne and Robert Taylor review three abstracts for us, all dealing with different aspects of phenotypical changes in the eutopic endometrium.

The countdown to WCE 2011 in Montpellier will soon start; it's just over a year away now. Start planning those last experiments (abstract submission starts on 31 September!), put a few more coins in the piggy bank each week to pay for the trip and contact all your friends to make sure they show up too! WCE2011 Congress President, Professor Bernard Hedon, has provided his first travel tips on page 8 to make it even harder to resist the temptation to head for the South of France in September 2011: science and tranquility at once …aiming for excellence. Isn't this what we are all about?

Oh yes: before I get carried away about the delights of the South of France in September, - if anyone is aware of new books that deserve to be scrutinised by our in-house book-reviewer, please let us know. We always – always! – welcome your input and feedback!

UPCOMING MEETINGS

19th Annual Meeting of the European Society for Gynaecological Endoscopy
29 September - 2 October 2010
Barcelona, Spain

International Pelvic Pain Society's 18th Annual Scientific Meeting, "Re-Thinking Chronic Pelvic Pain Evaluation and Management"
21 - 24 October
Chicago, USA

66th Annual Meeting of the ASRM
23 - 27 October 2010
Denver, USA

39th Annual Meeting of the AAGL
8 - 12 November 2010
Las Vegas, USA

Fertility Society of Australia's Annual Meeting 2010
10 - 13 October 2010
Adelaide, Australia

13th biannual meeting of the International Gynecologic Cancer Society (IGCS 2010)
23 - 26 October 2010
Prague, Czech Republic

Neuroendocrinology and female reproduction
28 - 30 October 2010
Venice, Italy

The 10th International Symposium on GnRH: The Hypothalamic-Pituitary-Gronadal-Axis in Cancer and Reproduction
6 - 8 February 2011
Salzburg, Austria

COMPLETE CONGRESS SCHEDULE

© 2010 World Endometriosis Society

Eutopic endometrial phenotypes in women with endometriosis

Dr Aimee S Browne MD MSc and Professor Robert N Taylor MD PhD
Division of Reproductive Endocrinology and Infertility
Emory University School of Medicine
Atlanta, Georgia 30322
USA

robert.n.taylor@emory.edu


Dr Aimee Browne

Professor Robert Taylor

Introduction

Endometriosis is defined by the presence of extrauterine foci of endometrial tissue and it affects up to 15% of women of reproductive age. Its etiology remains unknown. Sampson's theory of retrograde menstruation provides a mechanism for access of endometrium into the peritoneal cavity. However, it inadequately explains why only a minority of women with menstrual reflux into the coelomic space experience invasion and establishment of ectopic implants. Some researchers have focused their attention on the peritoneal environment ("soil"), whereas others have evaluated the eutopic endometrium ("seed") in an effort to identify factors that predispose women with the disorder to develop endometriotic lesions (Griffith et al, 2010).

We have selected three informative studies that highlight alternative approaches to understanding the regulation of cellular growth in the eutopic endometrium, and report how that process might be differentially modulated in women with and without endometriosis.

Increased expression of anti- to pro- apoptosis regulating genes in eutopic endometrium of women with endometriosis

It was Kerr et al (1972), who first described programmed cell death and coined the term "apoptosis" to describe this form of cellular shedding as the 'dropping off of leaves from trees.' It was shortly thereafter that the phenomenon was documented in menstrual human endometrium (Hopwood and Levison, 1976). Endometrial stem cells proliferate, whereas senescent cells undergo apoptosis. It has been hypothesized that dysregulation of this process promotes hyperplasia and other types of endometrial pathology, including endometriosis.

The cellular effects and consequences of apoptosis versus necrosis differ fundamentally, and may be critical for the maintenance of cyclical cellular homeostasis within the uterus. Apoptotic cell death is associated with characteristic nucleosomal cleavage and DNA degradation, whereas mitochondria and membranes remain relatively intact. By contrast, necrotic cell death is associated with substantial membrane and mitochondrial destruction with general sparing of the nucleus. The former pathway results in less inflammatory response and facilitates scavenging and clearance of menstrual debris.

Dmowski et al (2001) were among the first to suggest that impeded eutopic endometrial apoptosis might predispose to enhanced viability of shed menstrual fragments and implantation of endometriotic lesions. However, this finding has not been observed universally (Beliard et al, 2004).

The first study we will consider, by Braun et al (2007), uncovered differences in expression of apoptosis-regulating genes in the eutopic endometrium of women with endometriosis compared to those without disease. Quantitative, virtually multiplexed transcript abundance (VMTA) assays, based on reverse transcription-polymerase chain reaction (RT-PCR) technology, were used to measure the relative concentrations of several pro-apoptotic gene mRNA transcripts as well as those representing anti-apoptotic genes.

The authors' findings support the hypothesis that ectopic endometriotic lesions express much higher ratios of anti-apoptotic mRNAs (eg Bcl-$_X$L) to pro-apoptotic mRNAs (eg Bcl-$_X$S) than the endometrium of unaffected women.

The eutopic endometrium of women with endometriosis also showed an increased ratio of anti- to pro-apoptotic transcripts, with low levels of caspase-1 and p53 mRNA in the endometriosis subjects.

Another difference that was highlighted between the groups was that while control subjects demonstrated ovulatory phase cyclicity of caspase-1 and p53, there appeared to be dysregulation or lack of response to hormones in the endometriosis group.

© 2010 World Endometriosis Society

Quantitative expression of apoptosis-regulating genes in endometrium from women with and without endometriosis

Fertil Steril 2007;87:263-8

Braun DP, Ding J, Shaheen F, Willey JC, Rana N, Dmowski WP

OBJECTIVE: To quantitate antiapoptotic and proapoptotic gene expression in endometrial cells (ECs) of women with and without endometriosis. DESIGN: Determination of transcript abundance (TA) of apoptosis-regulating genes in eutopic and ectopic endometrial cells. SETTING: Institute for the Study and Treatment of Endometriosis, Chicago, Illinois, and university-based research laboratories. PATIENT(S): Women with (n = 10) and without (n = 6) endometriosis. INTERVENTION(S): None. MAIN OUTCOME MEASURE(S): Quantitative virtually multiplexed transcript abundance measurement (VMTA) of the Bcl2, BclxL, defender against cell death-1 (DAD-1), BclxS, P53, Caspase-1, and proliferating cell nuclear antigen (PCNA) genes. RESULT(S): The TA ratio of antiapoptotic to proapoptotic isoforms of the Bcl-X gene favors survival in eutopic and ectopic ECs from women with endometriosis, but not control ECs. This was found throughout the menstrual cycle for ectopic ECs. Eutopic but not ectopic ECs also expressed increased TA of the antiapoptotic DAD-1 gene in endometriosis. Eutopic and ectopic ECs from women with endometriosis expressed decreased TA of p53 and Caspase-1 compared to ECs from women without endometriosis. Expression of these genes was not correlated with the proliferative state of ECs based on TA of the PCNA gene. CONCLUSION(S): Dysregulation in expression of pro- and antiapoptotic regulatory genes characterizes eutopic and ectopic ECs from women with endometriosis. These results are consistent with apoptotic resistance and enhanced survival of ECs in endometriosis.

Overall, this study supports the notion that eutopic endometrium in women with endometriosis is relatively resistant to apoptosis and this effect occurs constitutively across the menstrual cycle. The findings might explain, in part, the intraperitoneal persistence of tissue fragments arriving via refluxed menstruation among women with endometriosis and their ability to implant on and invade into the peritoneum.

Endometrial microRNAs provide a mechanism for altered expression of apoptosis-mediating genes

A second study, which focused on variations in levels of microRNAs (miRs) within the endometrium of endometriosis cases, may contribute to some of the aforementioned observations about cell proliferation. MiRs are small, noncoding RNAs that bind to complementary sequences in the three prime untranslated regions (3' UTRs) of target mRNAs and regulate gene expression by post-transcriptional gene silencing. This class of regulatory molecules was initially discovered in C. elegans and has only been appreciated as a common regulatory strategy over the past decade.

Burney et al (2009) performed a global miR microarray profile which was validated with real-time PCR. They analyzed four early secretory endometrial biopsy specimens from stage III-IV endometriosis cases and three, unaffected controls, matched for sampling in the early secretory phase.

The selection of this phase of the ovulatory cycle was based on the group's prior microarray analysis of the endometrial transcriptome, which implied a molecular dysregulation during the proliferative-to-secretory transition in eutopic tissue from women with endometriosis (Burney et al, 2007).

Six miRs were found to be differentially expressed by a factor of >50%, which was deemed *a priori* as a statistically significant difference ($P<0.05$).

Among these, three were confirmed by real-time RT-PCR to be significantly lower in the four endometriosis cases than the three controls. One of these, miR-9, which was noted to be down-regulated in the endometriosis group by 25-fold, potentially targets the anti-apoptotic gene Bcl-2. Thus, low miR-9 levels might disinhibit transcription of Bcl-2, preventing apoptosis and allowing for continued proliferation and potential implantation of eutopic endometrium in cases of endometriosis.

Extension of this observation to a larger population of subjects is warranted before definitive conclusions can be drawn.

Curiously, another target of mIR-9 is the fibroblast growth factor (FGF) receptor. This interesting candidate gene resides at the chromosome 10q26 locus, which has been implicated by sib-pair gene linkage analysis as a potential endometriosis susceptibility region (Treloar et al, 2005).

Taken together, both lines of evidence could be used to support the hypothesis that FGF signaling might be increased in the eutopic endometrium of endometriosis patients.

© 2010 World Endometriosis Society

MicroRNA expression profiling of eutopic secretory endometrium in women with versus without endometriosis
Mol Hum Reprod 2009;15:625-31

Burney RO, Hamilton AE, Aghajanova L, Vo KC, Nezhat CN, Lessey BA, Giudice LC

Endometriosis is a common gynecologic disorder characterized by pain and infertility. In addition to estrogen dependence, progesterone resistance is an emerging feature of this disorder. Specifically, a delayed transition from the proliferative to secretory phase as evidenced by dysregulation of progesterone target genes and maintenance of a proliferative molecular fingerprint in the early secretory endometrium (ESE) has been reported. MicroRNAs (miRNAs) are small noncoding RNAs that collectively represent a novel class of regulators of gene expression. In an effort to investigate further the observed progesterone resistance in the ESE of women with endometriosis, we conducted array-based, global miRNA profiling. We report distinct miRNA expression profiles in the ESE of women with versus without endometriosis in a subset of samples previously used in global gene expression analysis. Specifically, the miR-9 and miR-34 miRNA families evidenced dysregulation. Integration of the miRNA and gene expression profiles provides unique insights into the molecular basis of this enigmatic disorder and, possibly, the regulation of the proliferative phenotype during the early secretory phase of the menstrual cycle in affected women.

Enhanced neurogenesis in eutopic endometrium of women with endometriosis

Previous studies of peritoneal fluid in women with endometriosis showed high variability and failed to detect differences relative to controls in the concentration of FGF (Huang et al, 1996; Seli et al, 1998).

Despite its angiogenic and mitogenic activities, FGF has been generally ignored as a potentially important growth factor in endometriosis. However, the recent focus on endometrial nerves in cases of endometriosis has brought renewed interest to this neurotrophic growth factor (Nakahara et al, 1996).

As highlighted previously in this journal (Rombauts, 2009), researchers from the team of Ian Fraser have identified dramatically higher densities of sensory Aδ, sensory C, adrenergic and cholinergic nerve fibers in the superficial endometrium of women with endometriosis relative to those in unaffected women (Al-Jefout et al, 2009).

In a more recent report the Ian Fraser group point at another aspect of endometrial neurogenesis in endometriosis by demonstrating for the first time the presence of neuro-endocrine (NE) cells in human endometrial glands (Wang et al, 2010).

Their new study reveals a higher density of NE cells in the eutopic endometrium from women with endometriosis than observed in normal subjects.

The investigators chose two NE-selective markers, synaptophysin (SYN) and neuron-specific enolase (NSE) to stain these relatively rare cells. Specific staining for both proteins was confined within the glandular epithelium, whilst it was absent in the stroma.

The authors suggested that these endometrial NE cells might function as 'taste cells,' capable to respond to stimuli within the endometrial lumen and to transform it into a secretory response.

The authors have yet to document whether a correlative association of NE cells and endometrial nerve fibers are observed in women with endometriosis.

An important question that remains is whether the increased density of NE cells in the eutopic endometrium of women with endometriosis plays a role in its pathogenesis. NE cells secrete a variety of bioactive amines, potent molecules that can induce smooth muscle contraction and nociceptor activation. Both phenomena are postulated to lead to pain symptoms in affected women.

Conclusions

To summarize, the three studies we have reviewed are fundamentally similar in that they all focus on molecular and cellular changes within the eutopic endometrium that may distinguish women with endometriosis from unaffected individuals.

These studies highlight the body of evidence that is rapidly accumulating in support of the concept that intrinsic qualities of the endometrium ("seed"), from which most lesions are likely derived, play a critical role in the ability of lesions to implant, invade, proliferate, become innervated and vascularized, and ultimately elicit inflammatory host reactions that are characteristic of endometriosis.

© 2010 World Endometriosis Society

Neuroendocrine cells in eutopic endometrium of women with endometriosis
Hum Reprod 2010;25(2):387-91

Wang G, Tokushige N, Russell P, Dubinovsky S, Markham R, Fraser IS

BACKGROUND: Endometriosis is a common gynaecological disease, but the pathogenesis of endometriosis and pathophysiological basis for endometriosis-associated painful symptoms are still uncertain. Little is known about neuroendocrine (NE) cells in the uterus. METHODS: For this study, 38 premenopausal women with histologically diagnosed ovarian endometrioma or peritoneal endometriosis and 24 women without endometriosis were selected. Biopsy samples from eutopic endometrium were used for immunohistochemical staining to detect synaptophysin (SYN) and neuron-specific enolase (NSE) expression in women with and without endometriosis. RESULTS: There were substantially more NE cells of eutopic endometrium stained with SYN and NSE in women with endometriosis than in those without endometriosis (3.8 +/- 1.8 versus 0.5 +/- 0.7/mm2, $P < 0.001$, and 2.8 +/- 2.1 versus 0.4 +/- 0.6/mm2, respectively, $P < 0.001$). These cells were scattered in the epithelium of endometrial glands. At all stages of the menstrual cycle, the densities of NE cells stained with SYN and NSE were greater in women with endometriosis than in those without endometriosis ($P < 0.05$). CONCLUSIONS: These results suggest that NE cells in eutopic endometrium probably play some role in the pathogenesis or symptoms of endometriosis.

REFERENCES

Al-Jefout M, Dezarnaulds G, Cooper M, Tokushige N, Luscombe GM, Markham R, Fraser IS. Diagnosis of endometriosis by detection of nerve fibres in an endometrial biopsy: a double blind study. Hum Reprod 2009;24:3019-3024

Béliard A, Noël A, Foidart JM. Reduction of apoptosis and proliferation in endometriosis. Fertil Steril 2004;82:80-85

Braun DP, Ding J, Shaheen F, Willey JC, Rana N, Dmowski WP. Quantitative expression of apoptosis-regulating genes in endometrium from women with and without endometriosis. Fertil Steril 2007;87:263-268

Burney RO, Hamilton AE, Aghajanova L, Vo KC, Nezhat CN, Lessey BA, Giudice LC. MicroRNA expression profiling of eutopic secretory endometrium in women with versus without endometriosis. Mol Hum Reprod 2009;15:625-631

Burney RO, Talbi S, Hamilton AE, Vo KC, Nyegaard M, Nezhat CR, Lessey BA, Giudice LC. Gene expression analysis of endometrium reveals progesterone resistance and candidate susceptibility genes in women with endometriosis. Endocrinology 2007;148:3814-3826

Dmowski WP, Ding J, Shen J, Rana N, Fernandez BB, Braun DP. Apoptosis in endometrial glandular and stromal cells in women with and without endometriosis. Hum Reprod 2001;16:1802-1808

Griffith JS, Rodgers AK, Schenken RS. Reviews: in vitro models to study the pathogenesis of endometriosis. Reprod Sci 2010;17:5-12

Hopwood D, Levison DA. Atrophy and apoptosis in the cyclical human endometrium. J Pathol 1976;119:159-166

Huang JC, Papasakelariou C, Dawood MY. Epidermal growth factor and basic fibroblast growth factor in peritoneal fluid of women with endometriosis. Fertil Steril 1996;65:931-934.

Kerr JF, Wyllie AH, Currie AR. Apoptosis: a basic biological phenomenon with wide-ranging implications in tissue kinetics. Br J Cancer 1972;26:239-257

Nakahara Y, Gage FH, Tuszynski MH. Grafts of fibroblasts genetically modified to secrete NGF, BDNF, NT-3, or basic FGF elicit differential responses in the adult spinal cord. Cell Transplant 1996;5:191-204

Rombauts L. Diagnostic laparoscopy for endometriosis: less is more. WES e-Journal 2009;11(4):5-8.

© 2010 World Endometriosis Society

Seli E, Zeyneloglu HB, Senturk LM, Bahtiyar OM, Olive DL, Arici A. Basic fibroblast growth factor: peritoneal and follicular fluid levels and its effect on early embryonic development. Fertil Steril 1998;69:1145-1148

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. Hum Reprod 2006;21:782-787

Treloar SA, Wicks J, Nyholt DR, Montgomery GW, Bahlo M, Smith V, Dawson G, Mackay IJ, Weeks DE, Bennett ST, Carey A, Ewen-White KR, Duffy DL, O'Connor DT, Barlow DH, Martin NG, Kennedy SH. Genome-wide linkage study in 1,176 affected sister pair families identifies a significant susceptibility locus for endometriosis on chromosome 10q26. Am J Hum Genet 2005;77:365-376

Wang G, Tokushige N, Russell P, Dubinovsky S, Markham R, Fraser IS. Neuroendocrine cells in eutopic endometrium of women with endometriosis. Hum Reprod 2010;25(2):387-91.

ASRM RUN FOR REPRODUCTIVE HEALTH

The inaugural ASRM 5K Run and 1 Mile Walk for Reproductive Health will take place on Monday 25 October 2010 at 06:30am in Denver, Colorado, USA.

It will be a memorable experience for the ASRM 2010 Annual Meeting attendees, and participants will contribute to increasing public awareness of the ASRM, and ensure continued support of its initiatives.

The top three overall male and female runners, and the top male and female in each age group, will receive a customized medal. The top overall male and female 1 Mile Walker will receive a medal.

REGISTER HERE:
www.active.com/running/denver-co/run-for-reproductive-health-2010

CANNOT RUN YOURSELF?

Ana Matilde Ramos – one of millions of women with endometriosis – will do it for you in the Adidas 5K run on 5 September 2010 in London's Hyde Park.

Ana Matilde has chosen the **World Endometriosis Research Foundation (WERF)** as the charity she will represent during this run (which has 100s of charities represented).

Please consider supporting Ana Matilde and WERF in the quest to FUND RESEARCH IN ENDOMETRIOSIS.

Every $10 (or more!) donation makes a difference! Please take a minute to support Ana and WERF!

DONATE HERE:
www.justgiving.com/Ana-Matilde-Ramos

WES IS ITS MEMBERS

For the World Endometriosis Society to continue its work we are reliant on the support of our members.

Please don't forget to renew your membership – YOU are the Society!!

www.endometriosis.ca/renew.html

© 2010 World Endometriosis Society

WORLD CONGRESS ON ENDOMETRIOSIS 2011

WCE2011 is now only 12 months away.... what do the inhabitants of Montpellier do in September?

by Bernard Hedon, WCE2011 Congress President

They prepare for *la rentrée*, which means "the return", after two months of summer holidays. This includes for everyone, of course, the return to work but also, for the children, the return to school. The students 'celebrate' the reopening of the university, and Montpellier, being very much a university town (60,000 students compared with a total local population of 500,000), sees its life pulse follow the rhythms of the university with a new year starting in September and finishing the following June or July.

Although the *rentrée* could be a depressing period because it means the end of your holidays, everybody feels good and full of strength.

- Is it because you have had a good rest?
- Is it because, with a new working year starting, you need to get re-organised and you issue new resolutions and objectives?

It is more than that: the tourists are gone and at weekends the beaches are more attractive than ever, with the water still being warm and refreshing. The sky is blue and the days are still long enough to enjoy long evenings at the time of sunset.

The temperature outside is just perfect, both for your activities and your outdoor sport practice.

The air is light and the chirping of the crickets slowly fades away.

In the fields, the *rentrée* coincides with a busy and happy occupation: it is the right period to harvest the grapes and prepare the new vintage of wine.

It is very pleasant to observe the agility of the *colle de vendangeurs* (people who cut the grapes), the ballet of tractors bringing the grapes to the winery, but also to smell the perfume of the juices, not fully fermented yet, and to taste the red-coloured liquid and try to imagine the sort of wine you will get after two years of maturation.

Blue skies? The *vignerons* (vine-growers) hope for a long-lasting period of good weather in order to let the grapes fully ripen and be able to harvest in the best possible conditions. But a number of fanatics look to the sky hoping for rain: the mushroom gatherers. They save a few days of their holidays to get away when requested by the *sortie*, the mushroom outing.

On these days, they get up very early, because they want to reach the woods before anyone else. They hide, because they do not want to reveal what they think is the best spot. They spend the day looking down, turning over stones and leaves with their wooden stick, and they will refuse to tell anybody where they have been and what they have been doing.

Only if you are very friendly, and if they have had a good outcome, will they lift their car trunk and, with intense pride, let you admire the result!

© 2010 World Endometriosis Society

Yes, September is a happy time in Montpellier.

By the way, it is exactly where, in twelve months, the WCE 2011 will take place!

Prepare to experience some of the unforgettable activities the Montpellier inhabitants enjoy at this time of the year.

You need tips?

Then, please, carefully read the next five issues of the e-Journal: you will find tips

- to visit wineries
- to go for cycling tours
- to admire monuments (Pont du Gard, Carcassonne, Nîmes)
- to trek in the midst of breath-taking scenery, or simply
- to rest in a seaside resort benefiting from the *arrière-saison* (the late season), far away from your own *rentrée*.

Keep up to date with the 11th World Congress on Endometriosis at **www.wce2011.com!**

MARK YOUR CALENDAR NOW

XIth World Congress on Endometriosis

WCE 2011

TOWARDS EXCELLENCE

Montpellier, France 4 - 7 September 2011

Abstract submission starts on 30 September 2010
What are you going to submit?

DEADLINE for contributions to the September/October e-Journal is 30 September 2010

© 2010 World Endometriosis Society