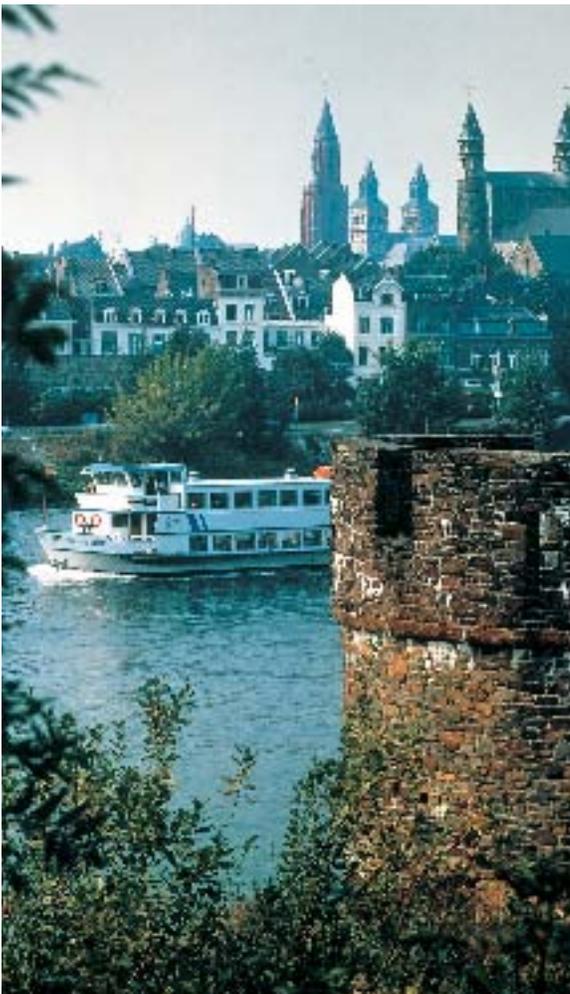




## Contents

- 1 • Editorial Maastricht - a City to Meet
- 2 • Upcoming conferences
- 3 • Trials on endometriosis treatment
- 3 • News
- 3 • New book
- 4 • Article: Adult Stem Cells in Human Endometrium - Possible Role in Endometriosis.
- 5 • Bibliography



## Editorial • Maastricht, a city to meet

Johannes L.H. Evers • Chair, local organising committee, 9th World Congress on Endometriosis, 14-17 September 2005, • Maastricht, The Netherlands

A lot has happened since the 8th world congress in San Diego in 2002. New treatments have been developed, new drugs are in the pipeline, and non-invasive diagnostic tests are on the horizon. The 9th World Congress on Endometriosis, which will be held from 14 - 17 September 2005 in Maastricht, The Netherlands, is promising to be very exciting. Over 375 abstracts have been submitted from 28 different countries. Surprisingly (or not?), Brazil is top scorer with 16% of the



abstracts, ahead of Japan with 12%, Australia with 9% and the USA also 9%. At the moment, around the world, most research is apparently focused on Endometrium (comprising 16% of the abstracts), Inflammation/Immunology (also 16%), and Surgical Therapy (16% as well). Research areas with less than 5% of abstracts submitted include Fecundity & Fertility (2%), Angiogenesis (4%), and Medical Therapy (4%).

The congress will present 11 seminars on topical subjects. Each seminar will be chaired by an international authority in the field, who will open the seminar with a state-of-the-art review of the world research so far. He/she will then proceed to introduce and discuss (together with the audience) 5 selected oral free communications on the topic of the seminar and, finally, open the seminar up for a general discussion. To conclude, the moderator will give his summary of the seminar and formulate targets for future research.

Basic and clinical researchers who have kindly agreed to moderate a seminar are Asgi Fazleabas (on: Endometrium), Paolo Vercellini (on: Epidemiology), Stephen Kennedy (on: Genetics & Genomics), Lone Hummelshoj (on: Pain & Quality of Life), Jean-Michel Foidart (on: Adhesion & Invasion), Robert Shaw (on: Medical Therapy), Robert Taylor (on: Inflammation & Immunology), Jacques Donnez (on: Surgical Therapy), Patrick Groothuis (on: Angiogenesis) and Rodolphe Maheux (on: Fecundity & Fertility). The final seminar will be moderated by Serdar Bulun and will address the important issue of "Translating emerging therapies into clinical practice".

Additionally 5 keynote lectures will be given on subjects sometimes only indirectly related to endometriosis: Chronic pelvic pain in the community, by Krina Zondervan (UK), Imaging, by Regina Beets (NL), Endometriosis pain from pelvis to brain, by Thomas Lundeborg (Sw) and Evidence-based Guidelines, by Andrew Prentice (UK). Linda Giudice (USA) will give this year's Special Guest Keynote lecture entitled "A Genomics Approach to Endometrial Function and Endometriosis".

Apart from all these "frontal" lectures and general discussions we aim to create an atmosphere in which ample opportunity will exist for informal exchanges of ideas and experiences. To facilitate this, quite some time will

## Upcoming Conferences

21st Annual ESHRE Meeting  
19 - 22 June 2005  
Copenhagen, Denmark

Endometriosis: Malattia Sociale  
22 - 25 June 2005  
Rome, Italy

38th Annual Meeting of the Society for the Study of  
Reproduction  
24 - 27 July  
Quebec, Canada

11th World Congress on Pain  
21 -26 August 2005  
Sydney, Australia

The First World Congress on Gender-Specific Medicine  
8 -11 September, 2005  
Berlin, Germany

• **The 9th World Congress on Endometriosis**  
14-16 September, 2005  
Maastricht, The Netherlands  
website: [www.conferenceagency.com/wce](http://www.conferenceagency.com/wce)

14th International Meeting of the European Society of  
Gynaecological Oncology  
25 -29 September 2005  
Istanbul, Turkey

15th World Congress on Ultrasound in Obstetrics &  
Gynecology  
25 - 29 September, 2005  
Vancouver, Canada

Endometriosis and Menstruation  
28 September - 1 October  
Villach, Austria

1st Beijing International Conference on Obstetrics and  
Gynecology  
7 -10 October, 2005  
Beijing, China

14th Annual Meeting of the European Society for  
Gynecological Endoscopy  
12 -14 October, 2005  
Athens, Greece

American Society for Reproduction, Annual Meeting  
15 -22 October  
Montreal, Canada

34th Annual Meeting of the American Association of  
Gynecologic Laparoscopists (AAGL)  
9 -12 November, 2005  
Chicago, USA

1st International Summit of the Society for Gynecologic  
Investigation  
10 -12 November, 2005  
Siena, Italy

Asia Pacific Congress on Egg Donation and Third Party  
Reproduction  
24 27 November, 2005  
Vizag, India

## Editorial (continued)

be set apart for discussions at the poster boards. Poster presentations are becoming more and more important as ways of exchanging scientific findings. Discussions at the posters allow eye-to-eye and ear-to-ear contact between presenter and participant, and on many occasions it is at the poster boards that new research ideas and collaborations evolve. For this reason, and to allow all participants to study all posters, and to allow the poster presenters to receive maximum exposure of their work, we will reserve a prime location for presentation of the posters and a prime time for discussion of the posters, during lunch in the main exhibit hall. The selected posters will remain on their boards for the entire duration of the meeting.



The city of Maastricht has a lot to offer. Its location at the heart of Europe makes it easily accessible by car, by train and by plane, for some even by bicycle. Hotel rooms abound and the medieval city centre offers abundant opportunities for dining and wining. In September, with some luck, it should still be possible to sit outside and enjoy a beer or a glass of wine on one of the many sidewalk cafés and enjoy a few hours of fun meeting old friends.

For an overview of the most recent updates of the scientific and social programs, please visit our website [www.conferenceagency.com/wce](http://www.conferenceagency.com/wce).

Also on behalf of Gerard Dunselman, Patrick Groothuis and Ton de Goeij, I hope to welcome you to Maastricht, on 14 September, at the opening reception of the 9th World Congress on Endometriosis.

Gezellig !



## **Trials on endometriosis treatment:**

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- 1: Doctors at Northwestern Memorial Hospital and Northwestern University's Feinberg School of Medicine, Chicago, USA are testing the effectiveness of an investigational drug, ERB-041, to relieve pelvic pain and inflammation due to endometriosis.
- 2: Doctors at the National Institutes of Health, Bethesda, USA are inviting women to take part in a pain relief study of a new treatment for endometriosis.

WES Members: Please contact the Wes e-journal if you wish to announce any new clinical trials or make any other news available to WES members.

Email [gillianh@nb.sympatico.ca](mailto:gillianh@nb.sympatico.ca)

## **NEWS**

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Endometriosis Awareness Week was observed 7-13 March, 2005 throughout Europe. Last year the European Endometriosis Alliance was formed, bringing together European endometriosis organizations for the first time. As a result it was decided to hold a common European Awareness week, linked to International Women's Day (8th March), with all member countries participating. Members lobbied politicians and campaigned the media and health professionals to raise awareness of endometriosis. A Written Declaration on Endometriosis was launched at the European Parliament in Brussels, which if signed by more than half the MEPs will ensure a reading in the Parliament and mean that endometriosis (as opposed to just 'women's health') will be on the Parliamentary agenda. Additionally many other special events took place throughout the continent in Austria, Denmark, Finland, Germany, Ireland, Italy, The Netherlands, Norway, Portugal, Spain, Sweden and the United Kingdom..

As part of the campaign to arouse awareness preliminary results from the Endometriosis Pain and Quality of Life Survey (run by the All-Party UK Parliamentary Group) were released. Unfortunately it appears that diagnosis times increased from 7 to 9 years, women are still living with pain for almost half the month, and endometriosis is severely impacting the lives of many who answered the survey. This survey may be accessed at: [www.endo.org.uk/aware2005-update](http://www.endo.org.uk/aware2005-update).

## **New Book**

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### **Dr Susan Evans. Endometriosis & Other Pelvic Pain**

Published by Lothian Books, 2005. (Paperback). Dr Evans is a laparoscopic surgeon who specialises in the treatment of endometriosis. She is a board member of the Australian Gynaecological Endoscopy Society. The book explains the medical and surgical aspects of endometriosis for patients, details treatment and describes how to get the most help from the health services. Co-author Margaret Taylor and Marsh cover complimentary therapies and suggest ways of living better with the disease.

## **Note**

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The e-journal is intended to be used as a vehicle of communication in the intervals between WES conferences. Members are encouraged to comment and discuss any topics related to endometriosis via the Discussion link. News about forthcoming meetings, moves or new appointments (anything you want other members to know about!) can be sent for inclusion in the e-Journal to the address below. Please remember that the e-Journal is published quarterly so we need information well in advance.

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# Adult Stem Cells in Human Endometrium - Possible Role in Endometriosis?

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The human endometrium shows remarkable regenerative capacity following menstruation, parturition, extensive curettage and hormone replacement therapy in postmenopausal women. During menstruation, endometrial glands and stroma regenerate from their remnants in the basalis to form the new functionalis layer, but little is known about the mechanisms involved. In other adult tissues, rare populations of adult stem cells with high proliferative potential have been identified that are responsible for regeneration and maintenance of the entire tissue during the lifetime of the individual. These adult stem cells occupy specific niches, are relatively quiescent, undergo self-renewal and uni- or multi-lineage differentiation, eventually producing numerous functional progeny. Cells derived from daughter progenitors have properties intermediate between their stem cell precursors and mature end-stage cells.

Adult stem cells are difficult to identify in tissues and are usually identified by demonstrating their functional properties. The classic approach is to examine a cell population for clonogenic activity, defined as the ability of a single cell to produce a colony when cultured at extremely low densities. We hypothesized that a small population of both epithelial and stromal stem cells residing in the basalis layer of human endometrium would exhibit clonogenic activity *in vitro*.<sup>1,2</sup> Using purified single cell suspensions obtained from hysterectomy tissue cultured at cloning densities, we demonstrated that  $0.22 \pm 0.07\%$  of endometrial epithelial cells and  $1.25 \pm 0.18\%$  of stromal cells formed individual colonies.<sup>1</sup> Two types of colonies formed for both epithelial and stromal cells. The large colonies were rare (0.09% of epithelial and 0.02% of stromal cells) and comprised small, densely-packed cells of high proliferative potential, initiated by putative endometrial adult stem cells.<sup>1</sup> The more common, small colonies were composed of large, loosely arranged cells of low proliferative potential initiated by more mature cells.<sup>1</sup> Further work has shown that the percentage of clonogenic epithelial and stromal cells in human endometrium does not vary significantly across the menstrual cycle, and that these clonogenic cells are also present in inactive, non cycling endometrium of peri-menopausal women or women taking oral contraceptives.<sup>3</sup> We have also identified 3 growth factors required for growth of colony-initiating epithelial cells, epidermal growth factor (EGF), transforming growth factor- $\alpha$  (TGFA) and platelet-derived growth factor -BB (PDGF-BB), and 4 for stromal cells, EGF, TGFA, PDGF-BB and basic fibroblast growth factor (bFGF).<sup>1,3</sup> Our current studies are investigating whether these clonally derived cells exhibit other stem cell properties. We are also attempting to identify specific markers of clonogenic endometrial cells, which would then enable us to determine their location in normal and pathological endometrium.

This data provides the first evidence for the existence of adult stem cells in human endometrium. It also suggests that the cells initiating the large, rare epithelial and stromal clones are endometrial stem cells that may be responsible for regenerating endometrial glands and stroma respectively. These putative stem cells are present in cycling endometrium throughout the menstrual cycle, and in inactive, non-cycling endometrium where they may have a role in regenerating endometrium of post-menopausal women treated with estrogen replacement therapy or in women ceasing oral contraceptives. We hypothesise that these putative endometrial stem cells may have a role in the development of gynaecological diseases characterised by abnormal endometrial growth.<sup>3</sup> Furthermore, we suggest that inappropriate reflux of these putative endometrial stem cells into the peritoneal cavity during menstruation may be responsible for the development and growth of endometriotic deposits in those women who develop endometriosis.

- Chan RWS, Schwab KE and Gargett CE (2004) Clonogenicity of human endometrial epithelial and stromal cells. *Biology of Reproduction* 70:1738-1750.
- Gargett CE (2004) Stem cells in Gynaecology. *Australian and New Zealand Journal of Obstetrics and Gynaecology* 44:380-386
- Schwab KE, Chan RWS and Gargett CE (2005) Stem cell activity in human endometrial epithelial and stromal cells during the menstrual cycle. *Fertility and Sterility*. (in press)

## Bibliography: New Articles Published Since February 2005

---

1. Imaoka I, Kaji Y, Kobashi Y, Wada A, Honjo G, Hayashi M, Yoshida M, Matsuo M.  
Cystic adenomyosis with florid glandular differentiation mimicking ovarian malignancy.  
*Br J Radiol.* 2005 Jun;78(930):558-61.  
PMID: 15900064 [PubMed - in process]
2. Chalas E, Costantino JP, Wickerham DL, Wolmark N, Lewis GC, Bergman C, Runowicz CD.  
Benign gynecologic conditions among participants in the Breast Cancer Prevention Trial.  
*Am J Obstet Gynecol.* 2005 Apr;192(4):1230-7; discussion 1237-9.  
PMID: 15846210 [PubMed - indexed for MEDLINE]
3. American College of Obstetricians and Gynecologists.  
ACOG Committee Opinion. Number 310, April 2005.  
Endometriosis in adolescents.  
*Obstet Gynecol.* 2005 Apr;105(4):921-7.  
PMID: 15802438 [PubMed - indexed for MEDLINE]
4. Rosenthal DM, Cheung VY.  
Fallopian tube prolapse after laparoscopic resection of pelvic endometriosis.  
*Obstet Gynecol.* 2005 Apr;105(4):808-9.  
PMID: 15802409 [PubMed - indexed for MEDLINE]
5. Greer JB, Modugno F, Allen GO, Ness RB.  
Androgenic progestins in oral contraceptives and the risk of epithelial ovarian cancer.  
*Obstet Gynecol.* 2005 Apr;105(4):731-40.  
PMID: 15802398 [PubMed - indexed for MEDLINE]
6. Hirota Y, Osuga Y, Hirata T, Yoshino O, Koga K, Harada M, Morimoto C, Nose E, Yano T, Tsutsumi O, Taketani Y.  
Possible involvement of thrombin/protease-activated receptor 1 system in the pathogenesis of endometriosis.  
*J Clin Endocrinol Metab.* 2005 Jun;90(6):3673-9. Epub 2005 Mar 8.  
PMID: 15755869 [PubMed - in process]
7. L'Huillier JP.  
Endobronchial endometriosis Nd-YAG therapy vs drug therapy.  
*Chest.* 2005 Feb;127(2):684-5; author reply 685. No abstract available.  
PMID: 15706019 [PubMed - indexed for MEDLINE]
8. Darai E, Thomassin I, Barranger E, Detchev R, Cortez A, Houry S, Bazot M.  
Feasibility and clinical outcome of laparoscopic colorectal resection for endometriosis.  
*Am J Obstet Gynecol.* 2005 Feb;192(2):394-400.  
PMID: 15695977 [PubMed - indexed for MEDLINE]
9. Yagyu T, Kobayashi H, Matsuzaki H, Wakahara K, Kondo T, Kurita N, Sekino H, Inagaki K, Suzuki M, Kanayama N, Terao T.  
Thalidomide Inhibits Tumor Necrosis Factor- $\alpha$ -Induced Interleukin-8 Expression in Endometriotic Stromal Cells, Possibly through Suppression of Nuclear Factor- $\kappa$ B Activation.  
*J Clin Endocrinol Metab.* 2005 May;90(5):3017-21. Epub 2005 Feb 1.  
PMID: 15687330 [PubMed - in process]
10. Pelage JP, Jacob D, Fazel A, Namur J, Laurent A, Rymer R, Le Dref O.  
Midterm results of uterine artery embolization for symptomatic adenomyosis: initial experience.  
*Radiology.* 2005 Mar;234(3):948-53. Epub 2005 Jan 28.  
PMID: 15681687 [PubMed - indexed for MEDLINE]
11. Kataoka ML, Togashi K, Yamaoka T, Koyama T, Ueda H, Kobayashi H, Rahman M, Higuchi T, Fujii S.  
Posterior cul-de-sac obliteration associated with endometriosis: MR imaging evaluation.  
*Radiology.* 2005 Mar;234(3):815-23. Epub 2005 Jan 21.  
PMID: 15665220 [PubMed - indexed for MEDLINE]
12. Luk J, Seval Y, Kayisli UA, Ulukus M, Ulukus CE, Arici A.  
Regulation of interleukin-8 expression in human endometrial endothelial cells: a potential mechanism for the pathogenesis of endometriosis.  
*J Clin Endocrinol Metab.* 2005 Mar;90(3):1805-11. Epub 2004 Dec 21.  
PMID: 15613411 [PubMed - indexed for MEDLINE]
13. Harada M, Osuga Y, Hirota Y, Koga K, Morimoto C, Hirata T, Yoshino O, Tsutsumi O, Yano T, Taketani Y.  
Mechanical stretch stimulates interleukin-8 production in endometrial stromal cells: possible implications in endometrium-related events.  
*J Clin Endocrinol Metab.* 2005 Feb;90(2):1144-8. Epub 2004 Dec 7.  
PMID: 15585560 [PubMed - indexed for MEDLINE]
14. Bellehumeur, C, Collette T, Maheux R, Mailloux, J, Villeneuve M, Akoum A  
Increased soluble interleukin-1 receptor type II proteolysis in the endometrium of women with endometriosis.  
*Human Reprod* 2005, May 20(5): 1177-84