How is your sex life? Do you climax easily? Did you have good sex last night?

Embarrassing questions you say? How then is the sex life of your patients? How often do they have intercourse? Does it make them feel satisfied? Do they have enjoyable orgasms? Does pain affect the intensity of their orgasms? Simple enough questions. But are they also simple to ask? A little awkward perhaps? Do they make you feel uncomfortable? Uneasy?

What do we really know about the sex life of our endometriosis patients? We can check the scientific literature: entering “("Sexuality") OR "Sexual Behavior") AND "endometriosis"” into PubMed produces only 54 (mostly useless) hits, as compared to “Pain" AND "endometriosis", which produces over 1500 hits, and “Infertility” AND “endometriosis”, which produces more than 2000 hits.

Still, when I attended a recent meeting of the Dutch Endometriosis Patients Organisation, “Sexual problems and endometriosis” was voted the single most important topic to be addressed at their next meeting. Couples endure painful intercourse, women are afraid of their relationship going awry, men feel inadequate in supporting their partner, who clearly is in so much pain.

In one of the rare but brave attempts to shed some scientific light on the problem, Simone Ferrero and co-workers (Ferrero et al, 2005) found endometriosis patients to be less satisfied with their orgasm than controls. Intercourse was more painful, they therefore had sex less frequently, the pain decreased the intensity of their orgasm, and they even had to interrupt intercourse regularly because of pain. Complaints were particularly severe in patients with deeply infiltrating endometriosis, especially when the uterosacral ligaments were involved. Traditional intercourse isn’t everything though, and some couples have discovered alternative ways of a fulfilling sex life, but this takes quite some communication between partners and it turns out that endometriosis patients feel more embarrassed than others to discuss their sexual needs with their partner.

Paolo Vercellini and co-workers (Vercellini et al, 2010) urge for a multidisciplinary research approach addressing sexual functioning in women with moderate-to-severe endometriosis, partner effects, co-morbidities and the (long-term) outcome of medical and surgical interventions. So, kind people of the World Endometriosis Research Foundation (WERF), what about a call for more research in this forgotten field? After all, even "Economics" AND “endometriosis” returns 99 hits!

REFERENCES


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Another year gone by quickly...

Here it is: this is the last issue of the first decade of the 21st century AD.

It is only befitting then that this is a bumper issue with lots of interesting reads and information. Our president, Hans Evers, was on roll call this time and has provided us with a guest editor's digest in addition to his regular introduction. In his guest editor's digest, Hans looks for evidence that ovarian stimulation accelerates the recurrence of endometriosis. He also picks up the thread again from the last issue in which he provocatively challenged the view that endometriosis causes infertility. He now digs up some new evidence that suggests that such a causative link does indeed exist, even in women without adhesions or endometriomata.

Professor Guo brings us an interesting summary of the first First Asian Conference on Endometriosis (ACE I) held in Shanghai; and Deborah Bush (Endometriosis New Zealand) announces a new collaboration with Air New Zealand (see pages 7 and 8).

WES and WERF have jointly published a one-pager of “Endometriosis facts”, which is available online at www.endometriosis.ca/facts-about-endometriosis.pdf. It should make it easier for all of us to refer to when asked about the disease by patients and the lay press.

The fifth volume of the journal US Obstetrics and Gynecology has now been published. It includes a foreword by WES board member Professor Liselotte Mettler and a striking advertisement for WCE2011. WES has recently signed an agreement with Touchbriefings for their journal to be freely accessible to our members via the following link: www.touchbriefings.com/ebooks/A1q1te/usobsandgynreg5/ (see pages 10 and 11 for Lilo’s piece and the ad!).

In further breaking news, the International EndoGene Consortium (IEC) has announced the results of the first genome-wide association study (see page 6). This is great news and we hope to hear more about their work in Montpellier.

Last but not least, we thought we would ask our readership how well we are doing before the year is over. The timely production of the WES eJournal requires a significant amount of work from an enthusiastic team. We would like to hear from every one of you where the eJournal can improve. Please take five minutes to complete the survey by clicking on this link: http://www.surveymonkey.com/s/ejournal-survey

On behalf of the editorial office I wish you all the best for the festive season. For those in Europe, it looks like a very cold, White Christmas has arrived early. Let us all spare more than a thought for those less fortunate than us.

UPCOMING MEETINGS

Reproductive surgery in the 21st century and beyond (RCOG / ESHRE / ESGE)
1 - 2 February 2010
London, United Kingdom

Annual Scientific Meeting of the SGI
16 - 19 March 2011
Miami Beach, USA

World Symposium on Endometriosis
24 - 26 March 2011
Atlanta, USA

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

Endometriosis 2011: the science and surgery of deep disease
18 March 2011
New York, USA

9th Deutscher Endometriose Kongress
1 - 4 June 2011
Emmendingen, Germany

>> COMPLETE CONGRESS SCHEDULE
“Endometriosis and IVF and endometriosis” is the theme I have chosen for this contribution to the Guest Editor’s series. My objective is to dig deeper into the question whether endometriosis per se affects fertility, but first to draw your attention to the other issue incorporated in the title: does IVF affect the development of endometriosis, does it activate occult lesions to become manifest, and manifest lesions to worsen and cause complaints?

In other words: all these artificial COH cycles that we are performing in our endometriosis patients, for IUI, for IVF, are they harmless? Is it really true that high oestrogen levels will not affect this most archetypical of oestrogen-dependent diseases at all?

A genuinely important question, but so far no firm answers. Until very recently there was only one single study to offer some insight into the problem. In 2006, Thomas D’Hooghe and co-workers from Leuven showed that the cumulative endometriosis recurrence rate is lower after high-dose ovarian stimulation for IVF than after lower-dose ovarian stimulation for IUI, suggesting that temporary exposure to very high E2 levels in women during ovarian hyperstimulation for IVF is not a major risk factor for endometriosis recurrence, at least if compared to IUI stimulation.

Apart from this study only a few case reports have been published, most of them documenting an increase in severity of endometriosis after ovarian hyperstimulation, such as for IVF.

Obviously the risk of publication bias is substantial here, for who would publish a case if endometriosis were not to increase?

Very recently, two studies appeared, although in rather obscure journals. Both are from Italy. Maria Coccia and her team from Florence and Rome (2010) published a retrospective cohort study of the (ultrasonographically detected) recurrence rate in 177 patients. There was no difference in recurrence between patients who underwent ART following laparoscopy for endometriosis and those who did not. Recurrence of endometriosis was defined as the presence of endometriotic lesions observed through TV-US.

Does controlled ovarian hyperstimulation in women with a history of endometriosis influence recurrence rate?

Coccia ME, Rizzello F, Gianfranco S

BACKGROUND: Endometriosis is a common estrogen-dependent disease. The aim of this study was to assess whether controlled ovarian hyperstimulation (COH) for assisted reproductive technology (ART) was associated with an increased incidence in endometriosis recurrence as documented by transvaginal ultrasound (TV-US).

METHODS: In a retrospective cohort study of 592 patients submitted to laparoscopy for endometriosis, 177 with infertility-related endometriosis who underwent a periodic ultrasound follow-up after laparoscopy were selected. Women who started ART after laparoscopy (n = 90) were compared with the control group, who did not undergo ART (n = 87). Recurrence of endometriosis was defined as the presence of endometriotic lesions observed through TV-US.

RESULTS: During a long-term TV-US follow-up (1-15 years), 40 (22.6%) recurrences were observed. Patients submitted to ART showed a cumulative recurrence rate similar to that of the control group (28.6% and 37.9% respectively, p = 0.471). Recurrent lesions were ovarian cysts (47.5%), ovarian nodules (37.5%), and rectovaginal disease (15%). The stratified analysis based on stages of endometriosis and pelvic pain did not show differences.

CONCLUSIONS: Gonadotropin treatments do not seem to affect the natural history of endometriotic lesions. The most important prognostic factors in recurrent disease observed by TV-US seem to be the stage of endometriosis and the presence of pelvic pain at the time of the first laparoscopic treatment.
their initial laparoscopy and those who didn’t (37.9% and 28.6% respectively), however the groups comprised of only 90 and 87 patients, so a type II error cannot be excluded.

Retrospective observational studies are prone to confounding and bias, but they can serve to generate and test a hypothesis. In order to prove a hypothesis — or prove it wrong — more elaborate prospective study designs are essential.

Laura Benaglia and co-workers from Milano (2010) studied 189 women with endometriosis and their (mostly subjective) recurrence of disease following ART. They did not observe an association between recurrence rate and the number of IVF cycles, nor between recurrence and the ovarian responsiveness to stimulation. Specifically, neither the number of started cycles (from 1 to 4 or more), nor the number of oocyte retrievals, nor the number of embryo transfers impacted on the 36 months cumulative recurrence rate of endometriosis following IVF in endometriosis patients, although in the recurrence group women had started three or more IVF cycles in 66% as opposed to only 46% in the non-recurrence group. Another hefty type II error?

It is fitting to conclude that the important issue of endometriosis recurrence post aut propter IVF has not yet been solved. Moreover, it has not yet been addressed appropriately. Only three retrospective observational studies have been published so far.

There is a need for a large-scale long-term prospective cohort study comparing the recurrence of endometriosis between patients with and without IVF, studying the number of cycles, the number of ampoules of FSH administered, the number of follicles and/or oocytes obtained, and the number of embryo transfers with respect to the recurrence of endometriosis.

Anti-Müllerian Hormone (AMH) is cool nowadays. No reproductive medicine centre with any self-respect, can afford not to buy a test kit from one of the two companies selling them and put its patients to the test. Also endometriosis patients. Which brings us to the second part of the title: the question whether endometriosis per se, so without adhesions and without endometrioma formation (i.e. minimal and mild disease), or endometriosis surgery does affect fertility?

In my contribution to the previous issue of this e-Journal I already alluded to this important issue. IVF registries, both from the US and from Europe, failed to show any difference in outcome between women with endometriosis and women with unexplained infertility. Two recent AMH studies challenged the view that endometriosis does not affect fertility. Both used AMH as an index of ovarian reserve.

Mutlu Ercan and co-workers (2010), from Ankara, studied 47 patients before and after surgical removal of one or more endometriomas. The mean level of serum AMH decreased from 1.6 to 1.4 ng/ml. However, this reduction was not statistically significant. Another type II error probably, but the authors draw the (incorrect, see later) conclusion that endometriosis does not impair AMH levels and that surgery does not appear to cause damage to the ovary.

Omar Shebl and co-workers (2010) from Linz studied 459 patients, 153 with and 306 without endometriosis. They used a different AMH assay. The mean serum level was significantly lower in the endometriosis patients compared to the controls (2.8 ng/ml vs. 3.5 ng/ml; p<0.001).

In women with mild endometriosis (rAFS I-II), the mean AMH level was similar to the controls but a significant difference was found between women with severe endometriosis (rAFS III-IV) and the controls (2.4 ng/ml vs. 3.6 ng/ml; p<0.0001).

These data seem to suggest that follicle reserve is impaired in patients with advanced endometriosis and that surgery may decrease it even more. Starting COH for IUI or IVF in

The impact of IVF procedures on endometriosis recurrence


OBJECTIVE: In infertile women with endometriosis requiring an in vitro fertilization (IVF) procedure, the potential risk of an IVF-related progression of the disease remains a matter of debate. Thus, since available data on this issue are scanty and controversial, an observational study has been herein conducted in order to clarify this issue.

STUDY DESIGN: We recruited 233 women with endometriosis who underwent IVF cycles in our unit. Patients were contacted to assess whether they experienced recurrences of the disease after IVF. The main outcome was to evaluate the impact of the number of IVF cycles and the responsiveness to ovarian hyperstimulation on the likelihood of recurrence. Clinical characteristics of women who did and did not have a recurrence were compared.

RESULTS: One hundred and eighty-nine women were included, 41 of whom (22%) had a diagnosis of endometriosis recurrence. The 36 months cumulative recurrence rate was 20%. The number of IVF cycles and the responsiveness to ovarian hyperstimulation were not associated with the risk of disease recurrence. The adjusted OR for recurrences according to the number of started cycles was 0.92 (95% CI: 0.77-1.10) per cycle (p=0.35). The adjusted OR for recurrences in women with endometriosis surgery was 0.80 (95% CI: 0.40-1.58) (p=0.52).

CONCLUSIONS: IVF procedures do not seem to influence the likelihood of endometriosis recurrence.
endometriosis patients may require an adjustment of the starting dose of FSH. AMH may help to determine to which patients this dose adjustment would be relevant.

In conclusion, we are making progress, but only with small steps at a time. There are underpowered studies abound and robust study designs are lacking. Ovarian (hyper)stimulation does not seem to fuel the recurrence of endometriosis after surgery however, but surgery as such may affect the already-compromised ovarian reserve in patients with advanced endometriosis.

REFERENCES


**NEWS / ANNOUNCEMENTS**

**Genome-wide association study identifies variations in the DNA of women that predisposes them to developing endometriosis**

Senior researchers in the UK (Dr Krina Zondervan), Australia (Professor Grant Montgomery) and the USA (Dr Stacey Missmer) have announced the results of the first GWA study to give robust evidence of variations in the DNA of women with endometriosis, showing that moderate-to-severe endometriosis is significantly more genetically driven than minimal-to-mild disease.

The study, which has been published in *Nature Genetics* (Painter et al, 2010), involved more than 5,500 women with endometriosis (and >8,600 controls) and has identified two regions on chromosomes 7 and 1 that were found to be associated with the disease.

One of the senior authors, Professor Grant Montgomery of the Queensland Institute of Medical Research in Brisbane, summarises:

“Studies to date have established that endometriosis is heritable, but have not addressed genetic burden for different disease stages. The International Endogene Consortium has been able to conclude that moderate-to-severe endometriosis is significantly more genetically driven than minimal-to-mild disease, which has implications for how we research the condition further”.

This is great progress and we hope to hear more about their work in Montpellier!

**Research priorities in endometriosis**

And speaking of Montpellier: last year the first consensus paper on research priorities in endometriosis was published in *Reproductive Sciences* (by Rogers et al, 2009) following a workshop held in connection with the 10th World Congress on Endometriosis in 2008.

Together with WERF, the World Endometriosis Society is repeating the success in Montpellier in connection with WCE2011, with an all day workshop to be held on 4 September 2011 - strictly limited to a maximum of 50 participants.

The workshop will again be led by Peter Rogers, Professor of Women’s Health Research at the University of Melbourne Department of Obstetrics & Gynaecology, Australia.

To apply to attend, please send an email to: wes@endometrioisis.org with your name, affiliation and stating the two areas within the field of endometriosis, which you feel you "specialise" in.

Attendance will be confirmed in March 2011.
First Asian conference on endometriosis (ACE I) held in Shanghai
by Sun-Wei Guo, Professor at Fudan University, Shanghai, China

Asia is the world’s largest and the most populous continent, hosting 60% of the world’s current human population and, consequently, the largest human female population. Endometriosis is a debilitating disease with an enigmatic pathogenesis. With a prevalence of approximately 10% in women of reproductive age, endometriosis affects much more women in Asia than any other continent in the world and impacts negatively on economy and society.

In responding to this challenge, the First Asian Conference on Endometriosis (ACE I) was held from 16-17 October in Shanghai, China. Organised by the ACE Organisation (ACEO) currently consisting of scientists from China, Japan, Korea, Taiwan, and Turkey, this meeting was the first-ever gathering of Asian scientists and clinicians interested in endometriosis, adenomyosis, and endometrial biology. Echoing the theme of the World EXPO Shanghai, the theme of ACE I was “Better research, Better life”.

Attended by well over 400 participants from China, Korea, Japan, Taiwan, and Indonesia, the 2-day conference covered many areas in basic and clinical research in endometriosis. Professor Kutay Biberoglu of University of Gazi, the inventor of the B&B scale for measuring the severity of dysmenorrhoea, gave a keynote speech entitled: “Endometriomas: Is surgery necessary?” He presented evidence and argued that in many cases surgery is no better than expectant management and could be avoided.

Another keynote speaker, Professor Tasuku Harada of Tottori University School of Medicine, gave a talk entitled “NF-κB and endometriosis” in which he provided ample evidence for an important role that NF-κB plays in the pathogenesis of endometriosis. He also talked about the use of several novel therapeutic agents such as, dienogest, peroxisome proliferator-activated receptor-γ (PPARγ) agonists, and apigenin (a flavonoid) in treating endometriosis.

Professor Young Min Choi of Seoul National University College of Medicine also gave a keynote presentation on “the genetics of endometriosis”, recounting their decade-long search for genetic polymorphisms that predisposing women to endometriosis and presenting some promising findings. Professor Sean Tsai of the National Cheng Kung University, gave a keynote talk entitled “Prostaglandin E2 as the master of endometriosis”. Summarising his years of extensive and painstaking research, he wove in numerous findings from his lab and demonstrated that PGE2 is a major culprit in the pathogenesis of endometriosis. Professor Sun-Wei Guo of Fudan University gave a talk on “endometriosis-associated pains”, an area that has previously received little, but now increasingly more, attention.

Besides the keynote presentations and podium presentations, there were three mini-symphosia featuring endometriosis research in China, Japan, and Korea. In addition, many other participants also presented their research findings, some of which seemed clinically very promising.

Dr Masao Igarashi, Professor Emeritus of Yokota Maternity Hospital in Japan, talked about his novel transvaginal echo-guided injection treatment for adenomyosis, vaginal and deep endometriosis, and ovarian endometriosis with a danazol (DA), 3-ethyl pyridine (EP), or valproic acid (VPA) solution. He reported that the maximum thickness of the posterior or anterior myometrium of the adenomyosis was reduced by 12.5%, 23.5%, and 23.0%, respectively, in the 16 DA-treated, 34 EP-treated, and 13 VPA-treated cases. In addition, the pain severity, as measured by the visual analogue scale, in patients with adenomyosis was improved by 43.7%, 51.3%, and 53.8% in patients treated with DA, EP, and VPA, respectively.

The ACE will be held every two years, with alternating hosts. The ACE II will be held in Istanbul, Turkey, in 2012.
Endometriosis wellness programme in the workplace
by Deborah Bush, Chief Executive of Endometriosis New Zealand

Earlier this year Endometriosis New Zealand launched its first workplace wellness programme known as WISE (Workplace Issue Solutions for Endometriosis). This initiative joins the already successful menstrual health programme in schools ('me') and 'Patient Partnering' in hospitals, and is off to a roaring start.

Air NZ (one of New Zealand's largest employers) was the first corporate to adopt WISE. A one-off or series of wellness workshops designed for the workplace, the programme covers issues impacting on women's lives and fertility. Information is relevant to the workplace and home with topics including endometriosis, chronic pelvic pain, irritable bowel syndrome, other related disorders, and fertility.

The workshops provide solutions for the employer and the employee to help them find a suitable pathway through the challenges the disease can cause with the aim of improving health outcomes, productivity and workplace goals. The programme attracts a professional fee which is designed to be affordable and in accordance with workplace size.

WISE was tailored to suit Air NZ and its employees, and can be adapted to fit with any workplace or employment situation. A large department store, a mechanical workshop, and a sportswear and merchandise outlet have booked the programme for the final months of 2010.

Feedback from the Air NZ workshop was overwhelmingly positive. As a result, and due to the sheer prevalence and effect endometriosis has had on some staff, Air NZ has engaged Endometriosis NZ to provide further one-on-one clinics, for those who have opted for more help.

Wineries around Montpellier
by Bernard Hédon, WCE2011 president

Montpellier is in the heart of the largest wine-growing area in the world. Not only is the landscape shaped by the vines, but the heart of the people is filled with innumerable stories about vine growing, wine making and, last but not least, wine tasting. Do not start a conversation with me on this subject if you are in a rush!

I will now tell you the thousand years old story of my family.

A distant ancestor started my family's wine business in 985 AD in the small village of Cruscades in the Corbières (near Narbonne). The original vineyards are still there! The business too, but more than a business it is a passion. It is something you cannot take away from the people unless you are prepared to send them to the next life.

Oenotourism is becoming more and more popular. It can take different forms, from the quick visit to a winery, just to buy a couple of bottles, or to a more organised tour to get to know more about the work involved and the wines that are cultivated.

If in a hurry, being able to bring back home some bottles with an intimate knowledge of their provenance, is already a treat. Serving the wine to one's friends together with its story enhances the tasting so much. It is no longer wine drinking, it becomes something else: discussion, enjoyment, socialisation, a nice evening with friends!

But if you have the time, returning with a better knowledge of what is driving the people of Montpellier and which is
deeply embedded in the local culture should be the second most important reason you choose to come to Montpellier in September 2011. No prizes for guessing the first reason....

Here are some tips for your oenotourism tour(s):

A half day trip:

Go to Aniane (30 km from Montpellier). You have the wineries, you also have the garrigue landscapes and the famous typical village of Saint Guillaume le Désert.

The locals will tell you the story of Astérix le Gaulois who prevented the installation of Mondavy who wanted to turn the area in another Napa valley.

A full day trip:

The pic Saint Loup is a most famous terroir. You will end up in Faugeres and Saint Chinian, which are all famous names. But you might find it difficult to drive back after all the wine tastings, unless you do what you should do: spit in specially made "crachoirs" the mouthful of wine after tasting, and swallow only the most precious tastings.

The complete experience:

You could also wait for the end of the congress and come with me for one day to the Corbières!

Walking through the vineyards I will show you the various species and the techniques we use.

You will visit the winery and taste what I consider as the best wine in the world!

See you in Montpellier!