

have wide experience, the rate of vaginal fornix removal has significantly increased year on year (Matsuzaki *et al.*, 2009).

- (iv) We agree that 32 papers to date have documented clinical outcome after bowel resection anastomosis, however we disagree with the received wisdom that 'histologically proven recurrence rate' is 2.5%. We consider this highly unlikely, and in support of our argument we present studies by Anaf *et al.* (2009) and Roman *et al.* (2010) who report that bowel margins are not free of disease in >10% of cases, meaning that histologically proven recurrence (or persistence) is already in excess of 10% at the end of the surgical procedure.
- (v) In our opinion, the populations of women suffering from deep endometriotic nodules are not so different in Louvain and Leuven. Moreover, we have successfully used the shaving technique on numerous patients consulting us for a second opinion, having been told they need extensive surgery with bowel resection and possible colostomy at elsewhere. We also dispute Meuleman's view that 'long duration has to be balanced against the low rate of complications'. Bowel resection is demonstrably associated with a higher rate of complications and reducing the duration of surgery that will not decrease this rate (Donnez and Squifflet, 2010).

References

- Anaf V, El Nakadi I, De Moor V, Coppens E, Zaeleman M, Noel JC. Anatomic significance of a positive barium enema in deep infiltrating endometriosis of the large bowel. *World J Surg* 2009;**33**:822–827.
- De Cicco C, Schonman R, Craessaerts M, Van Cleynenbreugel B, Ussia A, Koninckx PR. Laparoscopic management of ureteral lesions in gynecology. *Fertil Steril* 2009;**92**:1424–1427.
- Donnez J, Squifflet J. Laparoscopic excision of deep endometriosis. In: laparoscopy and hysteroscopy techniques. *Obstet Gynecol Clin North Am* 2004;**31**:567–580.
- Donnez J, Squifflet J. Complications, pregnancy and recurrence in a prospective series of 500 patients operated on by the shaving technique for deep rectovaginal endometriotic nodules. *Hum Reprod* 2010;**25**:1949–1958.
- Donnez J, Nisolle M, Squifflet J, Smets M. Laparoscopic treatment of rectovaginal septum adenomyosis. In: Donnez J, Nisolle M (eds). *An Atlas of Operative Laparoscopy and Hysteroscopy*. Carnforth, UK: Parthenon Publishing, 2001,83–92.
- Kovoor E, Nassif J, Miranda-Mendoza I, Lang-Avérous G, Wattiez A. Long-term urinary retention after laparoscopic surgery for deep endometriosis. *Fertil Steril* 2011;**95**:803e9–12.
- Landi S, Ceccaroni M, Perutelli A, Allodi C, Barbieri F, Fiaccavento A, Ruffo G, McVeigh E, Zanolli L, Minelli L. Laparoscopic nerve-sparing complete excision of deep endometriosis: is it feasible? *Hum Reprod* 2006;**21**:774–781.
- Matsuzaki S, Houle C, Botchorsihvili R, Pouly JL, Mage G, Canis M. Excision of the posterior vaginal fornix is necessary to ensure complete resection of rectovaginal endometriotic nodules of more than 2cm in size. *Fertil Steril* 2009;**91**:1314–1315.
- Roman H, Loisel C, Resch B, Tuech JJ, Hochain P, Marpeau L. Delayed functional outcomes associated with surgical management of rectal endometriosis: giving our patients an informed choice. *Hum Reprod* 2010;**25**:890–899.
- Roman H, Vassilieff M, Gourcerol G, Savoye G, Leroi AM, Marpeau L, Michot F, Tuech JJ. Surgical management of deep infiltrating endometriosis of the rectum: pleading for a symptom-guided approach. *Hum Reprod* 2011;**26**:274–281.
- Slack A, Child T, Lindsey I, Kennedy S, Cunningham C, Mortensen N, Koninckx P, McVeigh E. Urological and colorectal complications following surgery for rectovaginal endometriosis. *BJOG* 2007;**14**:1278–1282.
- Squifflet J, Feger C, Donnez J. Diagnosis and imaging of adenomyotic disease of the retroperitoneal space. *Gynecol Obstet Invest* 2002;**54**:43–51.

J. Donnez* and J. Squifflet
Department of Gynecology,
Université Catholique de Louvain,
Cliniques Universitaires Saint-Luc,
Brussels, Belgium

*Correspondence address. E-mail: jacques.donnez@uclouvain.be
doi:10.1093/humrep/der099

Advanced Access publication on April 7, 2011

Oral contraceptives and endometriosis

Discours de la Méthode. Pour bien conduire sa raison...¹

Sir,

It is with great interest that I read Vercellini *et al.*'s (2011) paper, which presents the reasons for the systematic use of long-term medical treatment in women suffering from endometriosis. Vercellini *et al.* from Milan have a long-established record in the application of surgical wisdom (Vercellini *et al.*, 2006, 2009), but I believe that this last article stands out as one of the best I have read over recent years and warrants a wide press amongst physicians involved in the management of endometriosis.

They emphasise that hormonal treatment is the best currently available medical therapy, that it will probably remain so for the foreseeable future, and that there is sufficient evidence to strongly recommend it, whether in association with or as an alternative to surgery. They also suggest that monophasic contraceptive pills or low doses of norethisterone acetate taken continuously should be considered as reference comparators in all future randomized controlled trials on medical treatments for endometriosis. I would like to take this a step further by suggesting that, on ethical grounds, Institutional Review Boards and journal reviewers should no longer accept further studies on medical therapies for endometriosis which include a placebo arm.

As endometriosis is a chronic disease with a high recurrence rate the authors correctly state that administration of short-term medical therapies is not only ineffective but flies in the face of medical logic. While most surgeons would agree that repetitive surgical procedures must be avoided, what is necessary is the systematic recommendation of post-operative medical treatment in order to prevent endometriosis recurrences which require new surgery. These considerations impact the methodology of case-series studies that aim to evaluate the risk of recurrences following various surgical procedures, such as resection of deep infiltrating endometriosis and ovarian endometrioma excision. In these studies, accurate information about the duration of post-operative medical treatment is seldom, if ever, available. Since numerous young women take contraceptive pills to avoid unexpected pregnancies, the relationship between recurrence rate and surgical treatment is invariably confused by post-operative hormonal therapy

¹By René Descartes, *Discourse on the Method of Rightly Conducting One's Reason...*, 1637.

intake. It is for this reason that accurate information about the duration of post-operative hormonal treatment in each patient should be mandatory in all prospective or retrospective studies that focus on the surgical management of endometriosis. This would allow for the likelihood of post-operative recurrences to be estimated from two distinct survival curves one with a starting point at the time of surgery, and the other at the end of post-operative medical therapy.

The acceptance by surgeons that medical treatment should systematically be prescribed in order to suppress the development of small residual foci responsible for recurrences would allow further questioning as to whether extensive surgery and compulsive carcinologic resection of all endometriosis lesions is still mandatory, particularly in cases with a high risk of unfavourable post-operative functional outcomes (Roman *et al.*, 2010). We are some way from answering this question, but contributions such as those of Vercellini *et al.* lead me to believe that we are on the right track.

References

- Roman H, Vassilief M, Gourcerol G, Savoye G, Leroi AM, Marpeau L, Michot F, Tuech JJ. Surgical management of deep endometriosis of the rectum: pleading for a symptom guided approach. *Hum Reprod* 2010; doi: 10.1093/humrep/deq332.
- Vercellini P, Pietropaolo G, De Giorgi O, Daguati R, Pasin R, Crosignani PG. Reproductive performance in infertile women with rectovaginal endometriosis: is surgery worthwhile? *Am J Obstet Gynecol* 2006;**195**:1303–1310.
- Vercellini P, Crosignani PG, Abbiati A, Somigliana E, Vigano P, Fedele L. The effect of surgery for symptomatic endometriosis: the other side of the story. *Hum Reprod Update* 2009;**15**:177–188.
- Vercellini P, Crosignani PG, Somigliana E, Vigano P, Frattaruolo MP, Fedele L. 'Waiting for Godot': a commonsense approach to the medical treatment of endometriosis. *Hum Reprod* 2011;**25**:3–13.

Horace Roman*

Department of Obstetrics and Gynecology, Groupe de Recherche EA 4308 'Spermatogenesis and Male Gamete Quality', Rouen University Hospital, 1 rue de Germont, 76031 Rouen, France

*Correspondence address. Tel: +33-232-888-643; Fax: +33-235-981-149; E-mail: horace.roman@gmail.com
doi:10.1093/humrep/der085

Advanced Access publication on March 25, 2011

Reply: Oral contraceptives and the endometriosis domino effect

Sir,

We are grateful to Dr Roman for his interest in our article (Vercellini *et al.*, 2011) and for the debate he has stimulated. As emphasized by Dr Roman, long-term medical therapy with monophasic oral contraceptives (OC) or progestins may prevent or interrupt the endometriosis domino effect.

The typical story begins with fortuitous identification of a small ovarian endometrioma at vaginal ultrasonography performed for pain or routine control in a young woman. A laparoscopy is indicated and part of the ovary removed together with the pseudocyst. Post-operative medical treatment is seldom prescribed or used for a few months only. Owing to the ~10% annual endometrioma recurrence rate, this sequence of events may be repeated before the woman

seeks a pregnancy. Meanwhile, pain may worsen and symptoms as well as disease control may become more complicated because of post-surgical adhesion formation. If there is an unexplained failure to conceive, another laparoscopy is frequently considered mandatory to check pelvic conditions, excise residual endometriotic lesions, and confirm tubal patency. However, ovarian reserve might have been already damaged by previous surgical insults, tubal fertility impaired by spontaneous as well as iatrogenic periadnexal adhesions, and a further surgical procedure might have a marginal effect. At this point, IVF is usually suggested, but the patient is eventually deemed to be a 'poor responder' and, after unsuccessful attempts, chooses ovum donation. In the following years she will probably continue her surgical Calvary until a hysterectomy is ultimately undertaken. The story might appear at the end but, based on the opinion of experts, the patient subsequently decides to remove also the gonads, to prevent the 4-fold increase in risk of endometrioid ovarian cancer. However, the ovaries might be difficult to remove, as they are stuck under extensive and dense adhesions, and a tiny fragment of parenchyma may be involuntarily left behind. As a consequence, only the climacteric will definitively free our unlucky patient from the ovarian remnant syndrome.

What would have happened had this woman used an OC since the first consultation without performing a laparoscopy first? Neither surgical procedures nor iatrogenic ovarian damage before child seeking would have occurred; only one laparoscopy would have been performed just in case of infertility or, alternatively, IVF with a presumably preserved gonadal reserve and fair probability of conception; when pregnancy was no longer an issue, indefinite OC use with sufficiently good pain control and achievement of an acceptable quality of life; prevention of disease progression or recurrence; substantial reduction of ovarian cancer risk (Modugno *et al.*, 2004), and the safe attainment of climacteric. Long-term OC use is not associated with major adverse consequences (Hannaford *et al.*, 2010; Vessey *et al.*, 2010).

These descriptions define only the extremes of a shades-of-grey scale, particularly considering that OCs and progestins are not effective or not tolerated in almost one-third of patients, and that surgery, when correctly indicated, remains an important aspect of endometriosis treatment. However, situations like the one depicted above are not infrequent in referral centres.

Behind the clinical consequences of a life with endometriosis but without OCs, there are also economical aspects to be carefully considered. The remarkable burden on medical resources is also due to the high prevalence and recurrent nature of the disorder. If the various manifestations of the disease are not prevented or adequately managed, they could occur in a cascade fashion impoverishing already limited national healthcare systems. The overall cost of endometriosis (including analgesics, hormonal therapies, gynaecological consultations, hospital admissions, surgical procedures, days off-work and reduced productivity) is impressive and substantially higher than estimated costs of other chronic conditions (Gao *et al.*, 2006; Simoens *et al.*, 2007). Projection studies are needed in order to evaluate the impact of two different healthcare models for women with endometriosis, one based mainly on long-term management with OCs and progestins, and the other based mainly on surgical procedures targeted at lesion elimination. It would be interesting to compare the results not only clinically, but also in terms of global medical expenditure: how much money could be saved by extensive OC use and invested in precious research?