

Authors' response to the Letters to the Editors concerning the article by Meaddough et al: Sexual Activity, Orgasm and Tampon Use Are Associated with a Decreased Risk for Endometriosis

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We appreciate the opportunity to respond to the concerns raised by Mss. Guidone, Marvel, Ballweg and Quinn about our article which recently appeared in this journal [1]. As our introduction discussed, prior to our study the literature supported the notion that sexual activity during menses may lead to endometriosis and, as has been emphasized by these letters, tampons as a delivery vehicle for dioxin appeared to represent a risk factor for developing endometriosis. Therefore, if we were biased in any way prior to analyzing the responses to our questions, we would have leaned towards believing that early tampon use and/or orgasm during menses would have been more frequent in the respondents with endometriosis. We were as surprised as the authors of these letters to find that these opinions were not supported by our study.

*Methodologies*

The questionnaire (<http://info.med.yale.edu/obgyn/kliman/Endometriosis/Orgasm.html>) that formed the basis of our study was designed to address a number of the concerns raised in the accompa-

nying letters. Question 10 (the only question asking about tampon and pad use) stated 'What products do you *usually* use when you have your period (now or in the past)?' The possible answers were: (1) neither pads nor tampons; (2) only pads; (3) only tampons, or (4) pads or tampons. We did not, as is misstated in Ms. Ballweg's letter, ask only about 'product use in the last year.' As discussed in our paper, only when we separated the responses into the 'only tampons' and 'only pads' did we see a significant difference between the cases and controls. Since we asked about life-long practice, we conclude that these differences accurately reflect behaviors both before and after endometriosis began for the cases. Likewise, the questions related to sexual activities were not limited to any time period, but asked about life-long behaviors. We assumed that women would be divided into those that did have sex during their periods and those that didn't. Again, only when we analyzed our data by comparing those women who either never or frequently engaged in sexual activities during their menses – thus eliminating those women who changed their behaviors over time – did we see statistical support for our conclusion that frequent sexual activity during menses was associated with a decreased incidence of endometriosis. While it is always possible that asking the question in a different way, or asking a series of more detailed questions, might have produced different results, these are the tasks for future epidemiologic researchers of these subjects.

*Sampson's Theory*

To discount Sampson's theory simply on the basis that it was proposed almost 80 years ago is as unreasonable as discounting Einstein's 1905 Special Theory of Relativity simply on the basis that it was proposed almost 100 years ago. The rare occurrence of extrapelvic or even male endometriosis are both consistent with Sampson's theory of transplantation of endometrium – extrapelvic endometriosis may reach distant sites via hematogenous or lymphatic spread, and male endometriosis is only seen after iatrogenic displacement of tissue from an estrogenically stimulated prostatic utricle at the time of radical prostatectomy. To date, Sampson's transplantation theory remains the only scientifically validated method of creating ectopic endometrium, and retrograde menstruation appears to be the primary method of delivery to the pelvis. Since retrograde menstruation is very likely more common than endometriosis, other factors may be involved. However, the retrograde menstrual load may well be one of those factors.

*Tampons and Dioxin*

The authors of both of the above letters appear to believe that tampons contain and deliver dioxin to the women who use tampons and that this exposure is the basis for their endometriosis. However, at each point of this argument compelling data exist to refute this conclusion.

In his review of the literature up to 2001, Scialli found no support for dioxins in tampons or as the cause of endometriosis [2]. De Vito and Schecter went further and showed that tampons do not contain 2,3,7,8-tetrachlorodibenzo-p-dioxin – the most potent dioxin – and that there is 13,000–240,000 times less of the other dioxins than in dietary exposures [3]. Furthermore, there is no evidence to date that tampons containing dioxins result in any measurable delivery to reproductive tissues.

If we set aside these studies and, for arguments sake, assume that tampons in fact do contain dioxins, is there evidence that dioxins cause endometriosis in humans? Mary Lou Ballweg, cofounder and

president of the Endometriosis Association (EA), and Sherry Rier, vice-president of research of the EA, have sought to connect dioxin exposure to endometriosis ever since the first rhesus monkey exposed to dioxin was found to have developed the disease [4]. In spite of the enthusiasm for this hypothesis [5], no epidemiologic studies have supported this concept [6–8]. Most recently after a failed attempt to ‘bolster the hypothesis connecting dioxins and endometriosis,’ Birnbaum and Cummings in their January 2002 review of the literature were forced to conclude that ‘none of these studies has detected clear differences in exposure to dioxins between women with and without endometriosis’ [9].

The best evidence that low levels of dioxin exposure are not associated with endometriosis in humans comes from the long-term follow-up of an extremely high dioxin exposure in Seveso, Italy [10]. 601 women  $\leq$  30 years of age who were exposed to the highest known levels of dioxin – much higher than the Rhesus monkeys in Rier’s [11, 12] study – were followed for 20 years. Endometriosis was confirmed by surgery or ultrasound. The final report published in July, 2002, concluded that even high levels of acute exposure did not statistically significantly increase the incidence of endometriosis [10].

Finally, if tampons, with or without dioxin, cause endometriosis, then we should have found a decreased incidence of endometriosis in respondents who never used tampons. We found the exact opposite, suggesting minimally that tampons do not appear to cause endometriosis, and, as we have suggested, may even be protective by acting as a wick to facilitate removal of menstrual debris.

#### *Orgasm*

Although it may be true that women who develop endometriosis may be less likely to subsequently engage in sexual activities during menses, our study attempted to determine if women with a life-long history of frequent orgasm during menses were more or less likely to have endometriosis. Our study suggests that frequent orgasm during menses is not associated with an increased incidence of endometriosis; on the contrary, it may be protective for women who have not contracted the disease. Of course this is only initial epidemiologic information. More focused investigation of this issue will be needed to validate this surprising finding.

#### *Clinical Recommendations*

Taken together, our study does not support the conclusions that tampon use or frequent orgasm is associated with an increased incidence of endometriosis. Since we found the opposite, it is even possible that these behaviors may be protective.

We fully agree with our critics that further study is necessary, and that media reporting of a skewed version of the results (without the caveats we included in our report) is not in the best interest of our

patients. However, we do believe that publication of such information serves the public interest by spurring scientists to take the next step. It would have been intellectually dishonest, we believe, to hold back these results any longer because they were contrary to our expectations or until further investigations were completed, as this approach is never advantageous to the scientific community. Finally, we believe in presenting scientific inquiry in as unbiased a manner as possible: we have published our hypothesis, our methods, the results, and what we believe to be the shortcomings of the study. This is how scientific advancement occurs. To state that ‘this paper brings science no closer to that goal, and may in fact further muddy the waters with its ill-found conclusions’ itself smacks of bias. We choose to remain open-minded and call for further investigation to clarify these interesting and unexpected findings.

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