part of the therapy of acute VVC, especially in patients with recurrent VVC.[2]

Noverr and Fidel are concerned about the vaginal site from which biopsies were taken, the VIZ mid-side wall. This is the traditionally preferred site for obtaining vaginal yeast culture, recognizing the macroscopic appearance similarity of the vagina through 360° with regard to appearance, histology, and microbiome. In addition, there is a lack of access to the vaginal floor and ceiling because of the speculum blades used in examination. Clearly biofilm could be disrupted in the biopsy process, but to be absent to the extent it was, makes this extremely unlikely, and bacterial biofilm was clearly apparent and retained. It is true that extracellular matrix was not stained for.

It is critical to emphasize that one should not confuse macroscopic biofilm evident on catheters and in plastic wells containing *Candida* populations containing extracellular matrix with microscopic biofilm evident only in histopathological vaginal sections (eg, bacterial vaginosis), which is invisible to the naked eye.

Clinicians are experienced in separating the grayish white frothy vaginal discharge characteristic of BV from the clumpy white discharge, sometimes adherent and confluent, typical of VVC. The macroscopic white plaques seen in VVC, reflecting large populations of hyphae producing *Candida* microorganisms together with bound epithelial cells and debris, do not reflect or constitute biofilm. Discharge in our study is entirely irrelevant.

We agree that antifungal drug resistance has been infrequent in the past in women with recurrent VVC because of *C albicans*; however, the frequency has increased significantly as a function of fluconazole drug exposure[3] and unrelated to biofilm existence. Resistance may also emerge as a consequence of deep mucosal persistence of yeast organisms, an observation that deserves further study. ■

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REFERENCES

1. Swidsinski A, Guschin A, Tang Q, et al. Vulvovaginal candidiasis: histologic lesions are primarily polymicrobial and invasive and do not contain biofilms. Am J Obstet Gynecol 2019;220:91.e1–8.
2. Sobel JD. Recurrent vulvovaginal candidiasis. Am J Obstet Gynecol 2016;214:15–21.
3. Marchaim D, Lamanek L, Bheemreddy S, et al. Fluconazole-resistant Candida albicans vulvovaginitis. Obstet Gynecol 2012;120:1407–14.

 https://doi.org/10.1016/j.ajog.2019.04.018

Years of unjustified hypoestrogenism, fear, and stress will not improve the management of chronic pelvic pain!

TO THE EDITORS: Agarwal et al[1] should be congratulated for emphasizing that patients with severe chronic pelvic pain should be managed actively. Indeed, years of inadequate treatment, with the assumption that this pain is normal, is deeply frustrating for these patients. Chronic pain may have significant negative impact on a patient's quality of life, resulting in central sensitization, loss of self-confidence and trust in physicians, and making long-term management more difficult.

Some of these women have severe or deep endometriosis that may be identified clinically or with imaging techniques. Others may have superficial disease, which could be confirmed at laparoscopy, although this should not be the first option in teenagers. Even minimally invasive surgery is too invasive to manage minimal endometriosis, which is not always progressive and may heal during medical treatment or even spontaneously.[2]

The presumption of endometriosis should not be mandatory for the physician to propose adequate treatment of severe chronic pelvic pain in young patients without obvious or confirmed endometriotic lesions. Many of these patients do not have and will never have endometriosis. The menstrual disorder of teenagers (MDOT) study reported that almost 30% of teenagers thought that something was wrong with their period, and 21% reported severe pain and 47% moderate pain.[3] However, the prevalence of endometriosis is about 10% among women of reproductive age.

Overdiagnosing the disease using clinical criteria because a noninvasive diagnosis test is not available will have severe consequences. Treatment of "a supposed endometriosis" with high-dosage progestins or gonadotropin-releasing hormone agonist will likely result in years of unnecessary hypoestrogenism. Young patients will experience years of unjustified fear and anxiety about probable infertility induced by a "possible mysterious chronic disease" that cannot be cured. Fear will likely worsen the symptoms of these young patients as adolescents' pain involves a significant psychosomatic component.

Careful management of severe dysmenorrhea, using analgesics and amenorrhea obtained with continuous low-dosage contraceptive pills, is possible. If the goal is to prevent a spontaneous worsening of the disease, prevention of menstruation is enough.[4] Finally, the absence of a noninvasive diagnostic test does not demonstrate that the cause of endometriosis is permanent, that the number of lesions is constantly increasing, or that recurrences are unavoidable thus implying that deep hypoestrogenism may be indicated when endometriosis is "suspected" on clinical symptoms. ■

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REFERENCES

1. Agarwal SK, Chapron C, Giudice LC, et al. Clinical diagnosis of endometriosis: a call to action. Am J Obstet Gynecol 2019;220:354–64.
2. Evers JL. Is adolescent endometriosis a progressive disease that needs to be diagnosed and treated? Hum Reprod 2013;28:2023.
3. Parker MA, Sneddon AE, Arbon P. The menstrual disorder of teenagers (MDOT) study: determining typical menstrual patterns and menstrual disturbance in a large population-based study of Australian teenagers. BJOG 2010;117:185–92.
4. Brosens IA. Endometriosis—a disease because it is characterized by bleeding. Am J Obstet Gynecol 1997;176:263–7.

 https://doi.org/10.1016/j.ajog.2019.05.001

REPLY

Check for updates

Thank you for your letter entitled "Years of unjustified hypoestrogenism, fear, and stress will not improve the management of chronic pelvic pain!" The goal of our manuscript entitled "Clinical diagnosis of endometriosis: a call to action" [1] was to highlight the current unacceptable delay in diagnosis and to encourage a focus on pain, functioning, and quality of life, with or without a previous surgical diagnosis endometriosis. We agree with your statement "Even minimally invasive surgery is too invasive to manage minimal endometriosis, which is not always progressive and may heal during medical treatment or even spontaneously."

You mention that as a result of an empiric diagnosis of endometriosis, "young patients will experience years of unjustified fear and anxiety about probable infertility induced by a possible mysterious chronic disease which cannot be cured." We contend that years of pelvic pain without answers or a diagnosis is a far greater tragedy—one that leads to women seeking multiple medical opinions and tests often without diagnosis and effective improvement in pain, functioning, and quality of life. Such an existence has substantial negative psychological and other consequences.

We are not proposing a paradigm in which women will have to endure "years of unnecessary hypoestrogenism." On the contrary, we propose trying effective endometriosis medical therapy and, if it does not work, to consider more extensive and possibly more invasive investigation and management. As highlighted in our manuscript, by excluding common confounding diagnoses before making the clinical diagnosis of endometriosis and initiating therapy, one has a high likelihood of improving the patient's pain, functioning, and quality of life in an expeditious and relatively noninvasive manner. ■

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REFERENCE

1. Agarwal SK, Chapron C, Giudice LC, et al. Clinical diagnosis of endometriosis: a call to action. Am J Obstet Gynecol 2019;220:354–64.

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Bacterial vaginosis and the risk of human papillomavirus and cervical cancer

Check for updates

TO THE EDITORS: In response to the article titled "Vaginal dysbiosis and the risk of human papillomavirus and cervical cancer: systematic review and metaanalysis," we the authors believe that the findings of Brusselaers et al[1] potentially could support the theory that there is a causal link between vaginal dysbiosis and cervical cancer.