Introduction: A focus on the medical management of endometriosis

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In this views and reviews series of articles, we focus on the long-term medical management of endometriosis in lieu of surgery. The development of noninvasive biomarkers will facilitate the early diagnosis of endometriosis and early medical management. We discuss the use of oral progestin-only as first line treatment in place of oral contraceptives. Future medical treatments may be curative rather than simply suppressive or palliative. The section on surgery mainly pertains to failed medical management or specific types of endometriosis which require surgical excision. (Fertil Steril® 2017;107:521–2. ©2017 by American Society for Reproductive Medicine.)
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Endometriosis is a chronic illness usually associated with pelvic pain and infertility. Endometriosis may be progressive and the pain associated with the condition can become debilitating. The goal of management is early diagnosis and treatment to prevent more advanced stages of the condition, especially as there is data suggesting the diagnosis of endometriosis is typically delayed by 8 to 10 years. The gold standard for diagnosis is laparoscopy with biopsy and histological demonstration of ectopic endometrial tissue. A presumptive diagnosis of endometriosis can often be made on history if the patient has classical symptoms such as pain with periods that is not completely relieved by nonsteroidal antiinflammatory drugs, pain that begins a day or two before the onset of menses, and acquired or progressive dyspareunia or dyschezia. Medical management to suppress endometriosis and improve quality of life should be started once a presumptive diagnosis is made. This simple strategy, in my opinion, would go a long way in preventing many of the later complications that could occur with endometriosis, such as ovarian endometriomas, adhesions, and scarring with a frozen pelvis. However, since there is no cure for endometriosis, all present treatments involve long-term suppression of the condition and may have side effects. Therefore, a noninvasive marker of endometriosis, which could confirm a presumptive diagnosis and avoid the need for surgery would be reassuring for both physicians and patients.

The contribution by Ahn et al. in this issue's Views and Reviews outlines past and present efforts in the quest to find a noninvasive diagnostic marker. As pointed out by the authors, this goal is challenging because of the apparent heterogeneous nature of endometriosis and the concern that peritoneal, ovarian, or deep infiltrating endometriosis all appear to be phenotypically different.

Once the diagnosis, either presumptive or definitive, is made, long-term therapy is required as all present medical treatments of endometriosis are suppressive not curative. The use of combined estrogen and progestin oral contraceptives has been a standard of care for many decades, but in my opinion should no longer be considered as appropriate treatment for endometriosis pain. Oral contraceptive pills appear to be effective because they will prevent primary dysmenorrhea related to prostaglandin production and will thereby relieve, at least partially, the dysmenorrhea in patients with endometriosis. However, oral contraceptive pills generally do not eliminate nonmenstrual pelvic pain or other symptoms of endometriosis such as deep dyspareunia. Thus, after what appears to be an initial improvement, if endometriosis pain persists or increases, instead of moving to an effective medical treatment or to laparoscopy, a different contraceptive pill may be tried. This switching from

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one oral contraceptive pill to another results in a delay of diagnosis, which is exactly what we are trying to avoid in the management of endometriosis. It is my belief that oral contraceptive pills should no longer be used as first line treatment for endometriosis pain and should be replaced by oral progestin-only therapy. My article in this issue's Views and Reviews section discusses this in greater detail.

The review by Bedaiwy et al. outlines the effectiveness and safety of long-term medical management of endometriosis using progestins-only or gonadotropin-releasing hormone (GnRH) agonists with add back. Both of these treatments are associated with a large body of data demonstrating that they can completely eliminate pain, improve quality of life, and reduce the size of endometriotic lesions. Both progestin-only treatment and GnRH agonists are safe to use in women of any age and are effective long-term. In the case of GnRH agonists, Bedaiwy and colleagues make the case that add back therapy with progestins or low-dose estrogen/progestin is always required for long-term use and is effective in preventing bone loss without impairing the suppression of endometriosis.

Occasionally surgery is required and Singh and Suen's review outlines the present indications for surgery in patients with endometriosis. Surgery can determine if the diagnosis is correct in women in whom medical management is ineffective, and may be necessary in cases where medical management is not tolerable because of side effects. Deep endometriosis may be associated with bowel and urinary tract obstruction that may not be responsive to medical management. Since all present medical treatments for pelvic pain associated with endometriosis also suppress ovulation, they are counterproductive in relation to infertility. In this regard, surgery may have a place in improving the ability for spontaneous conception or in very severe cases of endometriosis to make the ovaries accessible for in vitro fertilization. Surgery for ovarian endometriomas requires special attention due to the risk of potential harm to ovarian reserve and future fertility.

Finally, the last review in this month's Views and Reviews section by Bedaiwy et al., explores future work into developing new treatments for endometriosis. Some of the treatments presently in development are improvements on current therapy including oral GnRH antagonists and selective estrogen or progesterone receptor modulators. However, especially in light of the fertility issues related to endometriosis, future therapies are being searched for that will manage pain symptoms without suppressing ovulation, or better still result in a cure rather than just temporary suppression of endometriosis. In that regard, immunomodulators and antiangiogenic agents are of interest. Obstacles to this research still involve lack of understanding of the pathogenesis and natural history of the disease.

In summary, it is our hope that the readers of *Fertility and Sterility* will find these Views and Reviews articles informative in regards to possible new diagnostics, reassuring that medical management of endometriosis can be safely provided long-term, and thought-provoking concerning the controversial and future alternatives to present management.