## **Alternatives to Hysterectomy**

Uterine fibroids or leiomyomas occur in approximately 20% to 50% of women in the reproductive age group, and they are the most common pelvic tumors in women (1-3). The frequency is higher in women in their thirties and forties. Figures from autopsy reports suggest that the frequency may be as high as 75% (4). The incidence is three to nine times higher in black than in white women, suggesting a genetic predisposition in certain individuals (5). The precise etiology of fibroids has not been established.

Symptoms associated with fibroids include abnormal uterine bleeding, particularly menorrhagia and hypermenorrhea, as well as pelvic pressure or pain, bloating, increased urinary frequency and constipation. Infertility, first–trimester pregnancy losses, placental abruption, pain, premature labor during the second and third trimester, fetal malpresentation, inertia and dystocia during labor may also be noted. In addition, postpartum hemorrhage and infection may be associated with uterine leiomyomas. However, many women with fibroids are completely asymptomatic.

As women delay childbearing, physicians will encounter with increasing frequency patients who wish to maintain their fertility in the presence of symptomatic fibroids. The American College of Obstetrics and Gynecology has long recommended hysterectomy when the uterine size exceeds that of a 12-week gestation (5). Recently, this recommendation, even in women who have completed childbearing, has been challenged with a proposal that symptoms should be the primary determinant of therapeutic intervention (6). Certainly, in women desirous of future fertility, removal of the fibroid (myomectomy) is the procedure of choice. Hysterectomy is therefore, reserved for women who are not candidates for myomectomy. In the United States alone, uterine leiomyomas are cited as the primary indication for hysterectomy in over 250,000 cases per year, accounting for well over \$1.2 billion in health care expenditures. However women are now increasingly seeking minimally invasive alternatives to hysterectomy, secondary to the desire for a shortened postoperative period and their desire to maintain their fertility.

Minimally invasive surgical alternatives to hysterectomy include, laparoscopic and hysteroscopic myomectomy, uterine embolization, surgically guided thermoablative techniques, such as myolysis and cryomyolysis and MRI guided focused ultrasound therapy (FUS). Current medical treatments for leiomyomas involve the temporary suppression of serum estradiol or progesterone by the use of gonadotropin-releasing hormone agonists or the progesterone antagonist RU-486. These medications are currently limited to short-term use because of their side effects related to steroid suppression (bone loss, adverse effects on lipids, impaired cardiovascular and/or neurological function). Therefore, development of safe and effective nonsurgical, minimally invasive, or preventative therapies for leiomyomas would provide tremendous health benefits for women.

The development of new options for patients in the future will certainly be based on a better understanding of the genetics and molecular biology of uterine leiomyomas. On the horizon is the use of microarray analysis which will enable the testing of many genes for differential expression and capitalize on the knowledge and map of the human genome project. Targeting specific genes involved in the development of leiomyomata may provide the impetus for new

therapeutic strategies. However, our current alternative therapies are limited to either hormonal suppression or minimally invasive surgical therapies that spare the uterus. In this talk, we will review those agents and modalities but focus primarily on the newest minimally invasive surgical modalities and hormonal modulators which are currently under investigation. Continued efforts to understand the role of hormones in the development of leiomyoma will allow for the development of newer less invasive treatment strategies, which will help decrease the negative impact of leiomyomata on a women's health.

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