



CLINICAL UPDATE

CURRENT TRENDS IN THE PRACTICE OF MEDICINE

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Inside This Issue

A Practical Approach
to the Treatment
of Subclinical
Hypothyroidism.....3

A 2-Day Pain
Rehabilitation
Program Focuses
on Functional
Restoration.....6

Evaluating and
Managing Pelvic
Pain While
Preserving Fertility.....7

A New Form of Robotic Surgery, a Less Invasive Alternative for Management of Tonsillar Cancer

The Challenge

Cancer of the tonsil or base of the tongue is now one of the most common oral cancers; it develops in an estimated 1 in 30,000 persons each year, and the incidence of this cancer is rising. Its demographics are atypical for cancer in that it tends to affect otherwise healthy young people in their 20s through 50s. Although the cause of this rise in tonsillar cancers is not known, current research focuses on a link with oncogenic human papillomaviruses.

Typical presentation involves discovery of a lump in the neck. Biopsy often reveals advanced cancer. The standard treatments are chemotherapy and radiation. These may not be well tolerated and offer low to moderate success rates with poor outcomes because of adverse effects, including dysphagia, speech impairment, wide incisions, protracted use of a gastric feeding tube, and considerable morbidity from the treatment alone. Whether standard treatment has been effective may not be evident for 3 or 4 months. Mayo Clinic head and neck surgery specialists sought to develop a new surgical

Points to Remember

- **Cancer of the tonsils or base of the tongue is now one of the most common oral cancers, developing in an estimated 1 in 30,000 persons each year.**
- **There is a rising incidence of this cancer in people younger than 50 years.**
- **The most common presenting symptom is generally a lump in the neck that proves on biopsy to be a metastasis from an advanced tonsillar cancer.**
- **A new, less invasive form of robotic surgery allows complete removal of the tumor and greatly reduces recovery time—90% of patients are able to swallow in 2 weeks.**
- **At Mayo Clinic, the 5-year survival rate after transoral removal of tonsillar cancer is 81%.**

approach that offers an equal or better cure rate than the medical approach, while reducing adverse effects and thus improving patient quality of life.

A New Approach

During the past 2 years, the Mayo Clinic head and neck surgery team has worked to improve an existing surgical robotics system that could greatly improve access to the tumors by providing a precise, flexible wrist action in tight spaces (Figure 1). Designed originally for use in operations of the abdomen and pelvis, the system has been successfully fitted with smaller robotic instruments and adapted for use in the mouth. The robotic arms allow flexibility and freedom of movement in small spaces such as the mouth and throat (Figure 2, on page 2). Two binocular cameras help project a 3-dimensional image



Figure 1. Tonsillar cancer before surgery.



Figure 2. The surgical robotics system offers improved access to the oral cavity and better maneuverability.

from the lighted instrument that can be visualized by the surgeon at the robotic command console. The cutting technology of this robotic system offers cautery, ultrasonic vibration (Figure 3), and laser. Currently, Mayo Clinic is 1 of 3 US medical centers to have extensive experience in this service. Advantages of this approach include excellent survival rates of transoral surgery and reduced recovery time, pain, morbidity, and complications (Table).

For More Information

To learn more about tonsillar cancer and Mayo Clinic's robotic surgery for tonsillar cancer or to refer a patient for evaluation, please call 507-538-1392.

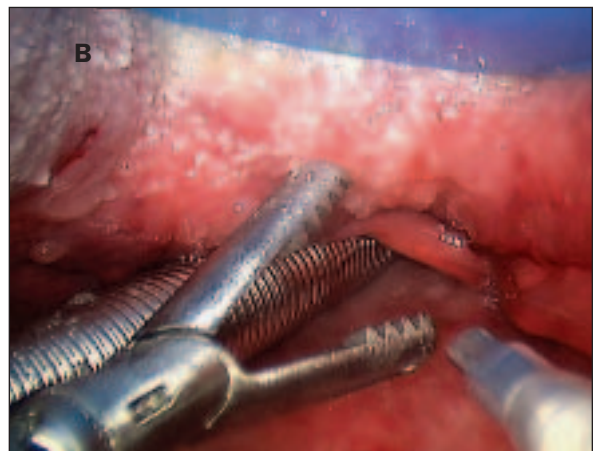
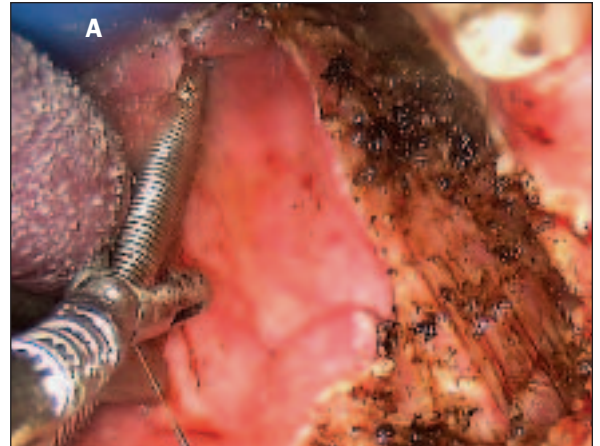


Figure 3. Intraoperative images of patient tonsil (A) and tongue (B). With the surgeon guiding the procedure from the command console, the robotics system provides binocular cameras that help project 3-dimensional images of tissue to be removed as the surgeon deploys a cutting tool.

Table. Advantages of Robotic Surgery for Tonsillar Cancer

<ul style="list-style-type: none"> • Total tumor removal • Ability to check margins in real time with the pathologist • Ability to remove neck lymph nodes • No need to use tracheotomy tube • No need to split the jaw and encounter extreme swelling and other complications • Ability to avoid cutting muscles and nerves • Reduced recovery time—80% of patients regain 	<ul style="list-style-type: none"> ability to swallow in 2 weeks, compared with the months required to do this after conventional surgery • Reduced hospitalization—patients go home in 2 or 3 days versus spending a week in the hospital after conventional surgery • Up to 80% of patients who undergo transoral tonsil cancer removal reach the 5-year survival mark, an outcome much better than that achieved with the standard approach
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A Practical Approach to the Treatment of Subclinical Hypothyroidism

The Challenge

Subclinical hypothyroidism occurs when the serum thyroid-stimulating hormone (TSH) level rises above the upper limit of normal (ULN) despite a normal serum free thyroxine (FT4) concentration. Subclinical hypothyroidism or mild thyroid failure is a common problem, with a prevalence of 4% to 8.5% in the adult population. The prevalence of subclinical hypothyroidism increases with advancing age and is higher in women (Figure).

Because serum TSH has a log-linear relationship with circulating thyroid hormone levels (eg, a 2-fold change in FT4 produces a 100-fold change in TSH), it is the key test for the diagnosis of subclinical hypothyroidism. Before diagnosing subclinical hypothyroidism, other causes of elevated serum TSH should be excluded. These include recovery from nonthyroidal illness, assay variability, heterophil antibodies, central hypothyroidism with biologically inactive TSH, and thyroid hormone resistance. However, the most common cause of elevated serum TSH is autoimmune thyroid disease.

Points to Remember

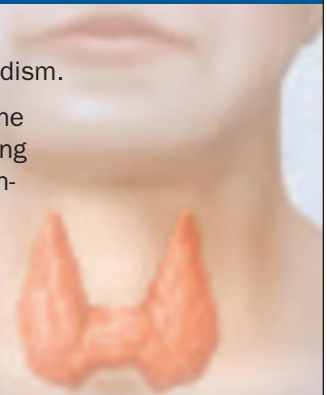
- **Subclinical hypothyroidism or mild thyroid failure is a common problem, with a prevalence of 4% to 8.5% in the adult population.**
- **Before diagnosing subclinical hypothyroidism, other causes of elevated serum thyroid-stimulating hormone (TSH) should be excluded.**
- **Many clinicians initiate thyroxine replacement therapy for all patients with TSH higher than 10 mIU/L, even if the free thyroxine level is within the normal laboratory range. However, this approach is controversial, as is whether patients with serum TSH levels between 5 and 10 mIU/L should be treated.**
- **To date, most studies have not shown an association of subclinical hypothyroidism with cardiac events and cardiovascular mortality.**

Table 1. At a Glance: Controversy Over Limits

Because of the large number of individuals potentially affected, there is a need to resolve the controversy over how to treat subclinical hypothyroidism.

- **Argument for lowering the ULN:** The strongest argument for lowering the ULN of TSH is the higher rate of positive antithyroid antibodies (reflecting underlying autoimmune thyroid disease) for individuals with TSH concentrations between 3 and 5 mIU/L and the higher rate of progression to clinical thyroid disease in this subgroup.
- **Argument against lowering the ULN:** The argument against lowering the ULN for serum TSH is that 22 million to 28 million additional individuals in the United States would be considered hypothyroid if the ULN of the TSH range were decreased to 2.5 to 3.0 mIU/L. Mayo Clinic data show that lowering the ULN of the TSH reference range to 3.0 mIU/L results in a 3-fold increase in the diagnosis of hypothyroidism in patients without a history of thyroid disease. Yet there is no evidence that intervention at these levels of TSH is beneficial.

Note of caution: Some evidence shows that lowering patients' serum TSH to the proposed new normal range by adjustment of the thyroxine dose does not improve their well-being or relieve their nonspecific complaints. For patients with TSH levels between 3 and 5 mIU/L, follow-up and possible measurement of thyroperoxidase antibody may be considered.



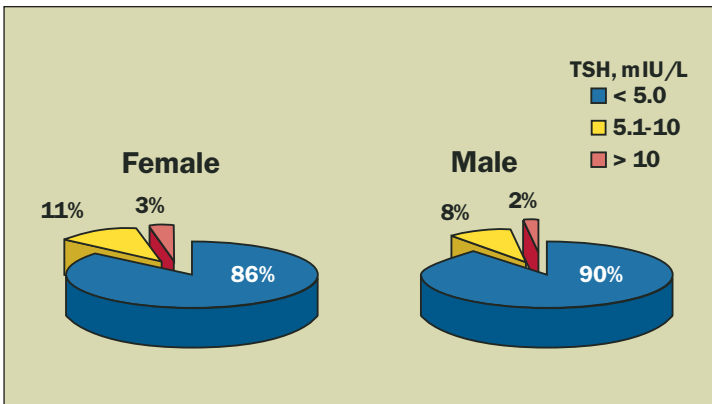


Figure. Serum TSH levels in 123,958 patients aged 50 years or older seen at Mayo Clinic, 1995-1997.

What Is the Upper Limit of Normal for TSH?

The ULN for serum TSH is the subject of hot debate (Table 1). The reference range used by Mayo Medical Laboratories is 0.3 to 5.0 mIU/L. However, data that support a move to lower the ULN of TSH to 3.0 mIU/L and possibly to 2.5 mIU/L have been published. These lower ULN cut-offs are obtained if individuals at risk of thyroid disease are excluded from the reference range population.

Should All Patients With Subclinical Hypothyroidism Be Treated With Thyroid Hormone Replacement?

There is consensus for initiating thyroxine

replacement therapy in patients with TSH levels higher than 10 mIU/L, even if FT4 is within the normal laboratory range. However, this treatment approach is somewhat controversial, as is whether patients with serum TSH levels between 5 and 10 mIU/L should be treated. The argument in favor of replacement therapy is based on numerous proposed consequences of untreated subclinical hypothyroidism: progression to clinical hypothyroidism, subtle systemic symptoms of hypothyroidism, lipid abnormalities, adverse cardiac end points, cardiac dysfunction, adverse fetal effects and pregnancy outcomes, possible contribution to infertility, neuromuscular dysfunction, psychiatric dysfunction, and cognitive dysfunction.

Several investigators have demonstrated subtle cardiovascular dysfunction in patients with subclinical hypothyroidism, but the clinical significance is questionable. To date, studies have not shown an association of subclinical hypothyroidism with cardiac events and cardiovascular mortality.

For More Information

To learn more about subclinical hypothyroidism or to refer a patient for thyroid evaluation, please call 800-313-5077.

Table 2. Clinical Approach Until More Evidence Is Available

Until guidance from carefully designed randomized trials becomes available, a practical approach is needed. Mayo Clinic physicians generally follow these guidelines:

- Individuals with serum TSH levels between 5 and 10 mIU/L should be treated selectively.
- Thyroxine replacement therapy should be reserved for patients who have goiter, women who are anticipating pregnancy or are pregnant, or patients with depression or bipolar disorder.
- Patient preference, clinical circumstance, age, presence of symptoms of hypothyroidism, thyroperoxidase antibody positivity, and level of and progression of TSH over time should also be considered.
- Subclinical hypothyroidism associated with autoimmune thyroiditis of children and adolescents should be treated.
- Mayo data show that patients with serum TSH levels higher than 8 mIU/L have a high likelihood of progression to TSH above 10 mIU/L in 4 years and may be considered for thyroxine replacement therapy.
- Improvement in serum lipid levels with thyroxine replacement therapy is more likely for patients who have baseline TSH levels higher than 10 mIU/L. If hyperlipidemia is encountered in a patient with a serum TSH between 5 and 10 mIU/L, specific lipid-directed therapy or lifestyle changes are needed.

Mayo Clinic Briefings

STUDY OF AORTIC DISTENSIBILITY AS MEANS OF PREDICTING ANEURYSM RUPTURE ACCEPTING ENROLLEES

Cardiac imaging researchers at Mayo Clinic Rochester are accepting enrollees for a 2-year study of aortic distensibility. The study is being done to develop radiographic software that will meet 2 goals: 1) to automatically measure the size and the pulsations of abdominal aortic aneurysm and 2) to determine if abdominal aortic pulsations may predict rupture or growth of abdominal aortic aneurysms.

Enrollment criteria include

- Age 18 to 99 years
- History of a confirmed or suspected abdominal aortic aneurysm of 4.9-cm diameter or less
- Absence of cardiac arrhythmias
- Body mass index of 31 or less

- Blood creatinine level of 2.0 mg/dL or less
- Absence of allergy to iodine or iodine-containing intravenous contrast dyes

Participants selected for this study will undergo computed tomographic angiography of their abdomen and pelvis. Testing involves placing an intravenous catheter in the arm to administer an iodine contrast during the scan and placing 3 electrode pads on the chest to monitor heart rhythm during scanning. Some participants may need to have blood drawn for a creatinine determination before scanning. Women of childbearing age may need to have blood drawn for pregnancy testing before scanning. Participants will be followed for 2 years or less should they have surgical treatment for their aneurysm.

For more information or to participate in this research study, please call 507-538-7109.

RELATIVES OF PARKINSON DISEASE PATIENTS FACE INCREASED RISK OF COGNITIVE IMPAIRMENT OR DEMENTIA

First-degree relatives of patients with Parkinson disease face greater risk of developing cognitive impairment or dementia than people who have no first-degree relatives (brother, sister, mother, father, son, or daughter) with Parkinson disease, according to a new study by Mayo Clinic investigators. The risk is particularly increased for relatives of patients who developed Parkinson disease before the age of 67 years.

The Mayo Clinic report appeared in the October 2007 issue of the journal *Archives of Neurology* (<http://archneur.ama-assn.org/>). It is one of the first large population-based studies to show that Parkinson disease and cognitive impairment or dementia may share familial susceptibility factors that make a person prone to developing one or both disorders. Results emphasize the clinical importance of taking careful family medical histories to accurately assess the risk of Parkinson dis-

ease a patient may face.

The study is based on the family study method, in which researchers assessed each relative separately for cognitive status instead of using only 1 family member to provide information for the full family.

The Mayo Clinic team studied

- 1,019 first-degree relatives of 162 patients with Parkinson disease from Olmsted County, Minnesota
- 858 first-degree relatives of 147 matched healthy controls from the same geographic area
- 2,716 first-degree relatives of 411 patients with Parkinson disease who were referred to Mayo Clinic from a broader area, including Minnesota, Iowa, Wisconsin, North Dakota, and South Dakota

Researchers emphasize that the familial susceptibility factors may be genetic or nongenetic, such as shared diet in the family. Further research is needed to determine susceptibility factors.

A 2-Day Pain Rehabilitation Program Focuses on Functional Restoration

Points to Remember

- Many clinicians are challenged by the comprehensive treatment necessary for patients with chronic pain.
- Multidisciplinary approaches combine pain reduction with instruction in coping strategies that teach patients to live and work with their pain.
- In 1974, Mayo Clinic was among the first medical centers to develop a 3-week multidisciplinary comprehensive pain rehabilitation program.
- A new 2-day program focuses on functional restoration to meet the needs of an emerging group of pain patients, many of whom are working professionals.

Patient 1

Four years after surgery for a back injury sustained in a car accident, a 56-year-old man is unable to return to his job as an accountant. He's tried all standard therapies and is beginning to lose hope that he'll ever manage his pain. He wants to know about going on permanent disability.

Patient 2

A 62-year-old grandmother has migraines that kept her from work so often she lost her job as a bank teller. Having tried all options, her physician finally prescribed narcotics. Now this patient finds herself too drowsy and fatigued to drive, make meals—even remember her children's telephone numbers.

Patient 3

A 34-year-old special education teacher contracted an unknown viral illness. Since the fever and headache cleared up, she has felt fatigue and aching and has difficulty sleeping and socializing. Recently diagnosed with fibromyalgia, she also is sad and depressed.

The Challenge

Managing a patient with chronic pain is difficult and one of the most frequently encountered frustrations of primary care medicine. As these patients exhaust management options, they seek more time with their physicians and become increasingly dissatisfied, placing physicians at risk of “burn out.” Many of these patients are working professionals who can benefit from short-term pain rehabilitation programs that teach them to live and work with their pain.

A Cognitive-Behavioral Model

In 1974, Mayo Clinic became one of the first multidisciplinary medical centers to develop a 3-week program at the Mayo Clinic Comprehensive Pain Rehabilitation Center (PRC). It is an intensive outpatient program focusing on functional restoration and improving quality of life.

The program consists of a multidisciplinary team of pain specialists who guide therapy in physical reconditioning, biofeedback and relaxation training, stress management, chemical health education, and activity moderation. Cognitive restructuring to decrease the sense of catastrophic pain and anxiety related to pain is also used. The most common diagnosis is chronic back pain, occurring in 24.5% of patients, but fibromyalgia is also quite common, accounting for 20% of patients. Other frequent diagnoses are chronic headache/migraines (11%), generalized pain or pain in multiple sites (7.5%), abdominal pain (7%), and neck pain (7%). The remaining 23% of patients have various pain sites, including upper or lower extremities, jaw, pelvic area, joints, and face, as well as postmastectomy and neuropathic pain. Patients using the program range in age from 13 years old to their early 90s.

The concepts taught at PRC by physicians, psychologists, nurses, physical therapists, occupational therapists, chemical health counselors, biofeedback therapists, and pharmacists include

- Learning to differentiate acute and chronic pain

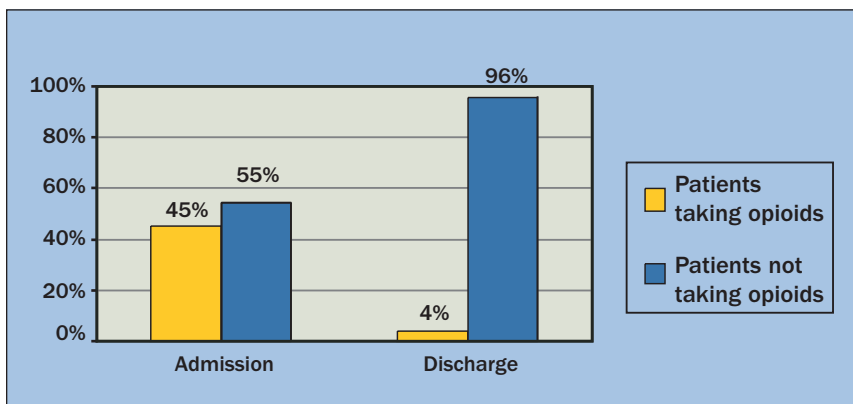


Figure. A goal of the 3-week pain program is discontinuation of opioids for pain while learning other cognitive-behavioral strategies to cope with persistent pain.

- Minimizing pain behaviors
- Using relaxation strategies
- Minimizing the use of analgesic pharmacotherapies (including narcotics as well as over-the-counter drugs)
- Engaging in daily exercise
- Using moderation in all activities
- Using stress management techniques
- Coping with the emotional aspects of chronic pain

An important goal of the 3-week program is the discontinuation of opioids for pain while learning other cognitive-behavioral strategies for coping with persistent pain (Figure). This approach has proven quite effective, with 73% of patients citing a decrease in their pain and 81% reporting an improvement in vitality at discharge.

A New Approach

Building on the success of the 3-week program, the same Mayo Clinic team of multidisciplinary spe-

cialists has developed a 2-day pain rehabilitation program called PREP. The 2-day program is indicated for patients who

- Have chronic pain
- Have exhausted medical and surgical options to “cure” pain
- Are ready for a program designed to help them live with their pain

As in the 3-week program, a cognitive-behavioral model serves as the basis for the 2-day program. The Mayo Clinic team evaluates each patient to determine whether the 3-week program or the 2-day program is suitable. Mayo Clinic specialists can also help with insurance certification.

For More Information

To learn more about the Mayo Clinic pain programs or to refer a patient, contact Mayo Clinic Pain Rehabilitation Clinic, please call 507-255-5921.

Evaluating and Managing Pelvic Pain While Preserving Fertility

The Challenge

Approximately 10% to 15% of all premenopausal women and 25% to 35% of infertile women experience pelvic pain and menstrual irregularities caused by endometriosis (Figure). There is a strong genetic component to endometriosis. A woman faces a 7-fold chance of developing endometriosis if her mother had endometriosis. Medical treatment consists of suppressing the menstrual cycle with oral contraceptives or more powerful medications. If this fails, the disease implants and adhesions often require open or laparoscopic surgical removal to relieve the symptoms. However, surgery poses the risk of infertility if excessive ovarian tissue and follicles are removed and adhesions form.

Treatment Options

Reproductive endocrinology specialists confirm a suspected diagnosis of endometriosis through laparoscopic examination and tissue biopsy. If a woman has completed childbearing or has no desire to bear children and wants to keep her

Points to Remember

- **Endometriosis is a cause of pelvic pain, infertility, and menstrual irregularities in approximately 10% to 15% of premenopausal women.**
- **If medical treatment fails to relieve symptoms, laparoscopic surgical removal of adhesions may be indicated.**
- **Ovarian endometriosis and surgery may endanger fertility because of the risk of destruction of the oocytes in the ovarian cortex.**
- **A multidisciplinary reproductive endocrinology practice can aid in the development of a complete fertility plan and is more experienced at conservative surgery, thus preserving fertility.**

pelvic organs, the focus of the pelvic examination is to determine areas of the pelvis that are most

To make an appointment for a patient through the Referring Physicians Service, use these toll-free numbers:

Mayo Clinic
Rochester
800-533-1564

Mayo Clinic
Arizona
866-629-6362

Mayo Clinic
Jacksonville
800-634-1417

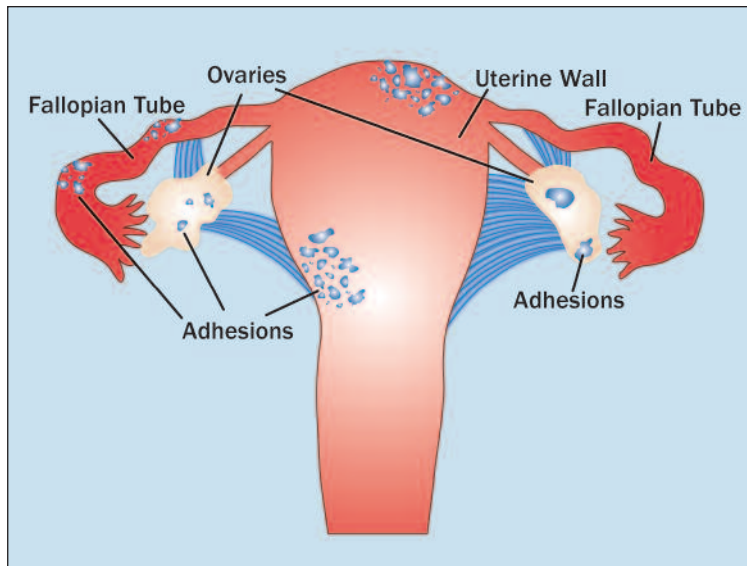


Figure. Endometriosis and distribution of adhesions. Pelvic pain and menstrual irregularities are common symptoms of endometriosis, an abnormal distribution of endometrial tissue in the reproductive tract. Severity of symptoms is not always related to the severity of the disease.

affected and to surgically remove the deposits.

If the woman desires to bear children—or the endometriosis is in locations too difficult to reach surgically—medical therapies may be used in conjunction with surgery. These therapies include continuous oral contraceptives or the use of injectable GnRH analogs to reduce estrogen production and thereby restrict growth of adhesions.

Medical therapy alone does not seem to markedly increase fertility.

Focus on Fertility

At Mayo Clinic, the multidisciplinary reproductive endocrinology team strives to preserve or improve fertility in several ways:

- Decreasing the amount of diseased tissue in the pelvis so natural fertility can return
- Using multiple methods to remove disease—through surgery, cautery, laser, and harmonic scalpel—to help minimize the chances of blocking or scarring to the fallopian tubes
- Precisely resecting ovarian adhesions to conserve ovarian tissue and follicles as well as reduce pain
- Working collaborations to help patients coordinate in vitro fertilization and maximize the number of oocytes (eggs) harvested

For More Information

To learn more about evaluation and treatment of endometriosis and Mayo Clinic reproductive endocrinology specialties or to refer patients for evaluations, call 507-284-9792

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Medical Editor
Scott C. Litin, MD

Science Writer
Anne D. Brataas

Production Manager
Carol F. Lammers

Production Designer
Connie S. Lindstrom

Manuscript Editor
Jane C. Wiggs



200 First Street SW
Rochester, Minnesota 55905
www.mayoclinic.org

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