Infertility

Although conceiving a child may seem to be simple and natural, the physiological process is quite complicated and depends on the proper function of many physiological processes, including the following:

- production of healthy eggs by the woman
- production of healthy sperm by the man
- uninterrupted passage through the fallopian tubes, allowing sperm to reach the egg
- the sperm's ability to fertilize the egg
- the egg's ability to interact with sperm and become fertilized
- the ability of the fertilized egg (embryo) to implant in the uterus

Who is affected by infertility?

The average probability of conception for a fertile couple having regular, unprotected intercourse is approximately 25% during each menstrual cycle. In most couples, conception occurs within 12 months of unprotected intercourse. It is estimated that infertility affects about 15% of couples of childbearing age.

How is infertility diagnosed?

When conception does not occur after one year of unprotected intercourse, or after six months in women over age 35, a medical evaluation of both the male and female is recommended. Some obstetrician/gynecologists are able to provide basic infertility evaluation and treatment. However, many causes of infertility are best treated by board-certified reproductive endocrinologists.

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Treatment for infertility

Once a diagnosis is made, our board-certified specialists can work with you to determine the best course of treatment based on:

- cause of the disorder
- your age, overall health, and medical history
- your tolerance for specific medications, procedures, or therapy
- expectations for your preferred course of care
- your opinion or preference

Yale Fertility Center
A PRACTICE OF YALE OBSTETRICS AND GYNECOLOGY

150 Sargent Drive, 2nd Floor
New Haven, CT 06511
203.785.4708 1.888.YALE.IVF
www.yalefertilitycenter.org

Office Hours: M-F 8:30am-5pm, with cycle treatment procedures 7 days per week, including evening hours by appointment

Female infertility

Causes of female infertility

In general, female infertility accounts for about 40% - 45% of infertility, while male infertility accounts for 35% - 40%. In 10% of cases both partners are responsible and in the remaining 10% there is no identifiable cause of infertility.

The most common causes of female infertility are:

- fallopian tube disease
- disorders of ovulation
- endometriosis
- decreased ovarian reserve
- multiple causes

Risk factors

Factors that can affect the ability to ovulate, conceive, or deliver successfully include:

- sexually transmitted disease
- fallopian tube disease
- hormonal imbalance (anovulation and abnormal menstrual cycles)
- endometriosis
- age: women in their late 30s are about 30% less fertile than women in their early 20s
- history of multiple pregnancy loss
- cervical intervention with cryosurgery or cone biopsy

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Risk factors (cont'd.)

- environmental factors: cigarette smoking, excessive alcohol consumption, or exposure to workplace hazards or toxins
- DES taken by the mother during pregnancy
- chronic diseases (diabetes, lupus, arthritis, hypertension, or asthma)

Options

- diagnosis and medical workup
- medications to induce ovulation including clomiphene citrate or gonadotropins
- reproductive surgery
- assisted reproductive technologies (ART) including *in vitro* fertilization (IVF) with or without intracytoplasmic sperm injection (ICSI)
- preimplantation genetic diagnosis (PGD)
- donor eggs/gestational surrogacy

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Male infertility

Male infertility is a sole or contributing cause in about 45% - 50% of infertile couples. Male infertility should be suspected when a man is unable to cause a pregnancy after 12 months of unprotected intercourse with a female who is ovulating and has patent fallopian tubes, or when a semen analysis shows low sperm count, low sperm motility, and/or a low number of normally shaped sperm.

Causes of male infertility

About 50% of males with low sperm count/low motility/low normal sperm have no identifiable cause for their infertility. The remaining 50% have one or more of the following:

- varicocele
- chromosomal abnormalities
- deletions in the Y chromosome
- androgen receptor gene mutations
- anatomical abnormalities
- immunological condition (antisperm antibodies)
- failed vasectomy reversal
- paraplegia
- ejaculation disorders
- cystic fibrosis
- hormonal imbalance (Kallman Syndrome, pituitary/hypothalamic disorders)
- liver disease, renal disease, thyroid disease, or treatment for seizure disorders
- hemochromatosis (iron regulation disorder)
- sickle cell disease

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Risk factors

- prostatitis, genital infection, or sexually transmitted diseases
- testicular trauma or torsion
- history of precocious puberty or delayed puberty
- exposure to toxic substances or hazards on the job, such as lead, cadmium, mercury, ethylene oxide, vinyl chloride, radioactivity and X-rays
- cigarette or marijuana smoking; use of illicit drugs
- heavy alcohol consumption
- exposure of the genitals to high temperatures
- hernia repair
- undescended testicles
- prescription drugs for ulcers, psoriasis, high blood pressure, ulcerative colitis
- DES taken by mother during pregnancy
- mumps after puberty
- chemotherapy or radiotherapy

Options

Treatment options may include drug therapy or surgery, or the following assisted reproductive technologies (ART):

- intrauterine insemination (IUI)
- *in vitro* fertilization (IVF)
- intracytoplasmic sperm injection (ICSI)

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Emotional counseling and support

”Emotional roller coaster” is a phrase often used to describe the ups and downs of infertility. As if the diagnosis and the treatment weren't difficult enough, the emotional turmoil surrounding infertility—while quite common—further exacerbates anxiety and stress. Psychological support and counseling can be very helpful to individuals and couples undergoing this process.

Although infertility affects approximately one in six couples in the United States, when faced with the diagnosis, most people feel isolated and alone. Especially difficult but normal feelings associated with infertility are:

- a loss of interest in usual activities
- difficulty thinking of anything other than one's infertility
- change in sleeping and/or eating patterns
- fleeting thoughts of death and dying
- difficulty making decisions
- feelings of isolation and loneliness

At times these symptoms may lead to strained relationships with one's partner, family, friends, and/or colleagues at work. An open (but entirely confidential) discussion with a counselor, such as our dedicated director of psychological services, Dorothy Greenfeld, MSW, LCSW, can often be quite helpful. In fact, infertile couples face a number of issues that can be addressed by meeting with a mental health professional.

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Dorothy Greenfeld, MSW, LCSW, director of psychological services, has been counseling individuals in all phases of reproduction for over twenty years.

Dorothy can provide important information about treatment options and help to facilitate discussion of such highly charged topics as whether or not to pursue a particular treatment; whether and how to pursue third party assistance (such as donor sperm, donor oocyte, and gestational surrogacy); and whether or not to pursue adoption. She can also help with questions about multiple pregnancy, pregnancy loss, and when and whether to stop treatment.

She is among the first assisted reproduction mental health professionals since the inception of IVF in 1982. Her expertise includes the emotional impact of infertility, pregnancy loss, multi-fetal pregnancies, ethical and psychological aspects of egg and sperm donation, and gestational surrogacy.

For more information on Dorothy, please visit
www.yalefertilitycenter.org/physician

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Endometriosis

Endometriosis is a common gynecologic disorder that affects over 4 million reproductive-age women in North America. In this condition, the lining of the uterus, or endometrium, grows outside of the uterus, typically in the pelvis surrounding the ovaries, uterus and fallopian tube. The two most common symptoms of endometriosis are pelvic pain and infertility. The pain often progresses as a woman enters her reproductive years; however, some women will have extensive endometriosis without any evidence of pain.

Endometriosis and infertility

- Endometriosis is one of the leading causes of infertility.
- Many women may not discover that they have endometriosis until they attempt a pregnancy.
- Endometriosis causes scar tissue and adhesions that can distort the reproductive organs and inhibit fertility. It also causes a generalized inflammation of the pelvis that prevents normal ovulation, egg transport, or fertilization.
- Many women with otherwise unexplained infertility are eventually diagnosed with endometriosis.

Treatment options

Yale reproductive endocrinologists offer both surgical and medical treatment options for women suffering from endometriosis.

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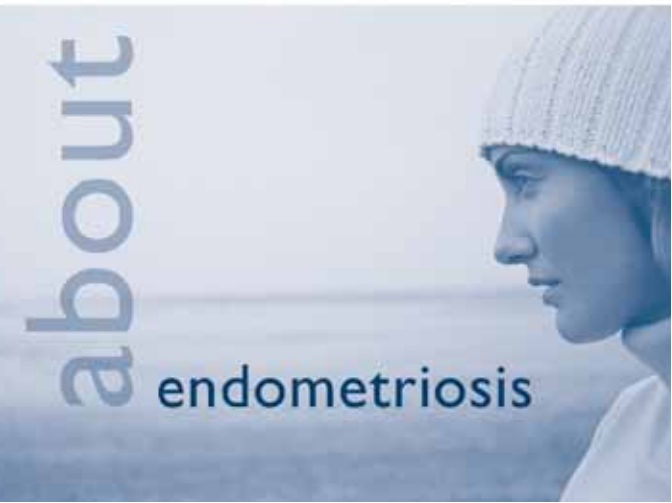

Surgery

Surgery removes or destroys the endometriosis. In most cases, surgery can be accomplished laparoscopically, without an overnight hospital stay.

Hormonal therapy

Several hormonal therapies may be used to treat endometriosis; however, all prevent conception, and therefore should not be used in someone who desires pregnancy. For women attempting to conceive, the most effective treatment is often the use of fertility medications. These medications will increase the chance of pregnancy even in the presence of endometriosis. The use of fertility-enhancing medications has an even higher success rate than surgical therapy to remove endometriosis. Pregnancy itself is also an excellent treatment for endometriosis.

Yale is a nationally recognized center for treatment of endometriosis. Our experts are available to diagnose this condition and treat both the associated pain and infertility.

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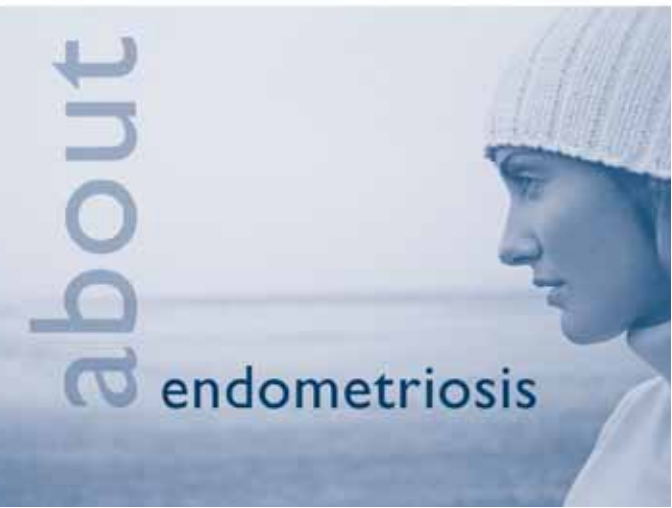

Intracytoplasmic sperm injection (ICSI)

Intracytoplasmic sperm injection (ICSI) is a micromanipulation technique developed to help achieve fertilization for couples with severe male factor infertility or couples who have had failure to fertilize in a previous *in vitro* fertilization attempt. The technique involves very precise maneuvers to pick up a single sperm and inject it directly into the center of a human egg. The procedure overcomes many of the barriers to fertilization and allows couples with little hope a chance to achieve a successful pregnancy.

The ICSI process

ICSI is a tool available in the IVF laboratory to achieve fertilization. The initial steps in preparation for ICSI are the same as for IVF:

- ovarian stimulation to produce several fertilizable oocytes (eggs)
- retrieval of the oocytes
- fertilization of mature oocytes with ICSI in the IVF laboratory
- placement of the embryos into the uterus for implantation (embryo transfer or ET)

What types of infertility can be helped by ICSI?

- extremely low sperm count and/or motility
- epididymal or testicular sperm only
- previous failed fertilization with conventional IVF
- high titer of antisperm antibodies

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In vitro fertilization (IVF) program

Yale Fertility Center is a recognized leader in the field of assisted reproductive technology. We launched the first *in vitro* fertilization program in the Northeast. The program started in 1982, and in 1983 the first Yale IVF baby was born to a couple who shared in our role as forerunners in this evolving field. The program offers support, information, and counseling, as well as the latest technological advances. We realize the process of overcoming infertility can be difficult; thus we try to minimize any uncertainty by thoroughly discussing all aspects of care.

In vitro fertilization - IVF

IVF involves fertilization in the lab by bringing together the sperm and oocyte and requires several steps:

- ovarian stimulation to produce several fertilizable oocytes (eggs)
- retrieval of the oocytes
- fertilization of the oocytes and culture of the embryos in the IVF laboratory
- transfer of the embryos into the uterine lining for implantation (embryo transfer or ET)

more ▶

What types of infertility might be helped by IVF?

- absent fallopian tubes or tubal disease that cannot be treated successfully by surgery
- endometriosis that is unresponsive to surgery or treatment
- male factor infertility, in which sperm counts or motility is low but there are enough active sperm to allow fertilization in the laboratory
- unexplained infertility that has not responded to other treatments
- chronic anovulation that has not responded to other treatments

Orientation to the program

We offer you an opportunity to meet our team of physicians and nursing staff, view a demonstration of injection administration, and tour our egg retrieval and embryo transfer areas. It is also possible to talk with others considering assisted fertility procedures or those who have already been through our program.

For further information, or to schedule an IVF consultation with one of our physicians, please call 203.785.4708.

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Natural cycle IVF / *in vitro* maturation (IVM)

With natural cycle IVF/IVM, patients avoid hormone therapy used in conventional IVF to produce large numbers of mature eggs at egg retrieval. Instead, immature oocytes are retrieved from the ovary and matured in the laboratory for 24 to 48 hours. Once the eggs have matured, fertilization is performed and fertilized eggs are then transferred to the uterus as in conventional IVF treatment.

Which women can benefit from natural cycle IVF?

IVM treatment is an important treatment option for women who want to avoid the inconvenience, cost and risks of gonadotropin therapy for ovarian stimulation. In general, the best candidates for IVM are women who:

- are under the age of 38
- have a large number of ovarian follicles seen on ultrasound
- have suffered from or are at increased risk of ovarian hyperstimulation syndrome
- repeatedly produce poor-quality embryos after conventional IVF
- are poor responders to hormone therapy

Procedure for natural cycle IVF

Natural cycle IVF/IVM treatment requires less time commitment compared to conventional IVF. Full treatment consists of two or three ultrasound examinations followed by an injection of hCG (human chorionic gonadotropin) to mature the eggs 35 hours prior to egg retrieval.

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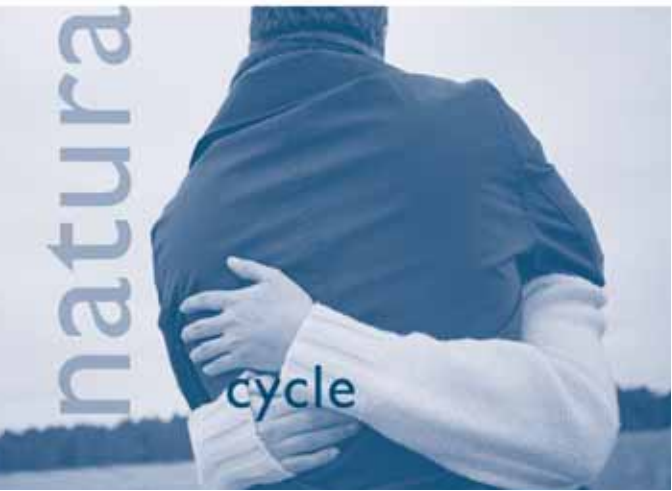

Following egg retrieval, immature eggs are cultured in a maturation medium for 24 to 48 hours and then mature eggs are fertilized using the intracytoplasmic sperm injection (ICSI) technique. Embryo transfer occurs two to five days after fertilization.

As with conventional IVF treatment, medications are given following egg retrieval in order to make implantation easier and to support the hoped-for pregnancy. Support of pregnancy is especially important in IVM treatment because the follicles that yield eggs (and would normally support pregnancy) are immature in IVM treatment.

Advantages of natural cycle IVF

The advantages of natural cycle IVF include:

- avoidance of ovarian stimulation with hormones and the associated cost and potential complications such as Ovarian Hyperstimulation Syndrome
- a simpler treatment protocol with fewer injections and ultrasonographic evaluations

Please call to schedule a consultation with one of our specialists to determine if natural cycle IVF may be a good option for you.

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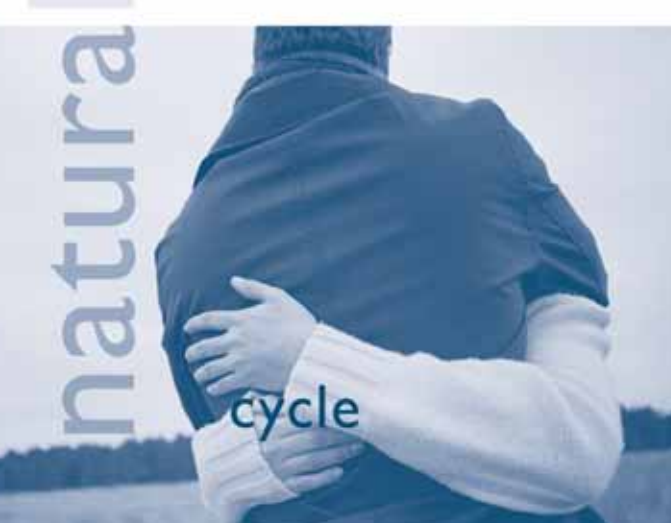

Preimplantation genetic diagnosis

Preimplantation genetic diagnosis (PGD) is a test that can identify chromosomal and genetic defects in embryos before they are transferred into the uterus. PGD is performed in conjunction with IVF, and is offered to both fertile and infertile individuals. PGD provides an earlier alternative to current postconception diagnostic procedures such as amniocentesis or chorionic villus sampling.

When can PGD help?

PGD may be of value in the following circumstances:

Advanced Maternal Age – women approaching the age of forty

Multiple IVF Failures – embryos may have an incorrect number of chromosomes

Recurrent Pregnancy Loss – miscarriages resulting from abnormal chromosomes

Chromosome Rearrangements – such as translocations that increase risk of miscarriage

Genetic Disease – such as cystic fibrosis, hemophilia, or muscular dystrophy

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How we perform PGD

The PGD process involves removal of a single cell from each embryo, followed by analysis of chromosomes or genes. This procedure does not harm the embryo. Analysis of the removed cell allows us to determine whether or not an embryo is healthy.

Testing chromosomes using PGD

To test for chromosomal abnormalities, the cell removed from the embryo is analyzed using a procedure called fluorescence *in situ* hybridization (FISH). PGD can help detect Down syndrome and other common chromosomal problems that could lead to birth defects or miscarriage. At Yale, we currently test for nine chromosomes.

Testing for genetic disease using PGD

To test for inherited diseases caused by mutation in a single gene, the cell removed from the embryo is placed in a test tube and the DNA is amplified using a process called the polymerase chain reaction (PCR). Once amplified, the DNA is tested to determine whether the disease-causing mutation is present. Only mutation-free embryos are transferred to the uterus and thus any pregnancy that results should be unaffected by the disease in question.

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Recurrent pregnancy loss

Approximately seventy percent of women who miscarry once or twice can expect to go on to carry a child to full term. But for those who experience three or more miscarriages, diagnostic testing and treatment may be needed to determine a cause and provide valuable clinical information for subsequent pregnancies.

Pregnancy loss can have multiple causes. The most common factors in repetitive miscarriages include:

- autoimmune problems
- genetic problems
- anatomical problems
- hormonal problems

A number of tests are used to determine the reasons for recurrent pregnancy loss. These include:

- chromosomal analysis of both partners
- examination of the uterine cavity via ultrasound
- immunological testing
- hormonal testing
- specific genetic testing

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The Recurrent Pregnancy Loss Program at Yale Fertility Center has a multidisciplinary team approach. A comprehensive evaluation and treatment plan, designed by a team including perinatologists, pathologists and psychologists together with reproductive specialists, allows for the broadest possible assessment of each patient.

Each patient in the program will be evaluated to establish a care plan specific to her individual needs. Second and third trimester treatment is offered in coordination with Yale Maternal-Fetal Medicine. The initial evaluation will include a visit with a perinatologist, with other consultants available as needed.

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Fertility preservation options

Who are candidates for fertility preservation?

- Women at risk for ovarian failure
  a. Cancer patients
  b. Patients with autoimmune (lupus) or hematologic (aplastic anemia) conditions treated with high-dose gonadotoxic chemotherapy
  c. Patients undergoing sterilizing surgeries for any reason (e.g., endometriosis surgery, prophylactic oophorectomy)
- Women who wish to delay motherhood

Fertility concerns for cancer patients

In the United States, approximately 800,000 men and women of reproductive age are undergoing cancer chemotherapy or radiation that may destroy eggs and sperm.

- Radiation causes the most severe damage to the ovaries or testicles.
- Chemotherapy drugs in the "alkylating agent" category, such as cyclophosphamide (Cytoxan®, Neosar®), mechlorethamine (Mustargen®), chlorambucil (Leukeran®), and melphalan (Alkeran®), also cause severe damage to both sperm and eggs.

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Because the first goal is always to cure the cancer, even if the treatment causes sterility, the Yale Fertility Center has developed a unique program, offering a variety of established and experimental options for fertility preservation in women and men.

For women, options include:

Embryo freezing – During this process, women undergo *in vitro* fertilization (IVF) and the embryos created are then frozen, using well-established protocols.

Repositioning of the ovaries – If radiation will be administered to the pelvis, the ovaries may be surgically repositioned out of the radiation field to reduce the risk of damage to the eggs.

Egg freezing – Following hormonal stimulation, eggs are retrieved, then frozen. While still considered experimental, more than 200 pregnancies have been reported worldwide using frozen eggs. With egg freezing, there is no need for a partner and no necessity for surgery.

For men, we offer:

Sperm freezing – Semen samples may be frozen before starting chemotherapy or radiation therapy, stored for years, and used later for insemination.

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Third party reproduction

Egg donation

The Yale Egg Donation Program, established in 1989, was one of the first programs of its kind in the Northeast. Oocyte (egg) donation allows women whose ovaries do not contain eggs (or contain eggs unlikely to result in healthy embryos) to become pregnant.

An increasing number of women are choosing egg donation programs when other traditional fertility procedures, including IVF, have been unsuccessful. It is also appropriate for women who were born without ovaries, whose ovaries have been removed or damaged, or who are now producing eggs with decreased viability due to advanced maternal age, premature menopause, or chromosomal abnormalities.

Our program offers a choice between anonymous and directed (known) egg donors. Anonymous donors for our program are healthy women between the ages of 21 and 33 who have passed a rigorous screening process, which includes extensive genetic and infectious disease screening, a thorough physical examination, a psychological assessment by the program counselor, and thorough cycle monitoring by the program coordinator. Final approval of the donor is made with the physicians, coordinator, counselor, and recipient couple.

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Embryo donation

This service provides the opportunity to conceive using embryos donated by patients who have previously undergone fertility procedures at the Yale Fertility Center. Once the donating couple, without identifiable genetic disease, has the number of children they wish, they may donate their remaining embryos to the Center for other infertile patients.

Gestational surrogacy

We help facilitate gestational surrogacy, an option for women who are unable to carry a pregnancy.

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Hugh S. Taylor, MD
Section Chief, Reproductive Endocrinology and Infertility
Specializes in IVF, reproductive surgery, congenital anomalies, diethylstilbestrol (DES) exposure, implantation/endometrial receptivity, uterine anomalies, endometriosis, polycystic ovarian syndrome (PCOS), recurrent pregnancy loss (first trimester), and fibroids.

Aydin M. Arici, MD
Specializes in egg donation, gestational surrogacy and third party reproduction, endometriosis, fibroids, reproductive surgery, and recurrent pregnancy loss (first trimester).

Gabor B. Huszar, MD
Director, Sperm Physiology Laboratory
Specializes in sperm function tests, donor insemination, and sperm cryopreservation prior to vasectomy.

Pasquale Patrizio, MD, MBE
Director, Yale Fertility Center
Specializes in female and male infertility, assisted reproductive techniques (IVF, ICSI, PESA, TESE), preimplantation genetic diagnosis (PGD), egg donation and gestational surrogacy, reproductive surgery, and reproductive options for women and men with cancer.

Beth W. Rackow, MD
Specializes in polycystic ovarian syndrome (PCOS), endometriosis, menorrhagia, and endoscopic surgery.

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Emre U. Seli, MD
Director, Donor Egg and Gestational Surrogacy Program
Specializes in IVF, reproductive surgery, advanced endoscopic surgery, reproductive options for women with cancer, endometriosis, menstrual disorders, dysfunctional uterine bleeding, polycystic ovarian syndrome (PCOS), hirsutism, and menopause.

Denny Sakkas, PhD
Director, Embryology Laboratory
Specializes in male infertility (ICSI), embryo culture, and preimplantation genetic diagnosis (PGD).

Dorothy Greenfeld, MSW, LCSW
Director, Psychological Services
Specializes in third party reproduction (egg donation and gestational surrogacy) and a full range of psychological services for infertile couples.

For more information on our specialists, please visit *www.yalefertilitycenter.org/physician*

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From I-91 traveling south from Hartford
Travel south to merge of I-91 and I-95.
Continue on I-95 to exit 46/Long Wharf Drive.
Turn left off exit ramp onto Sargent Drive.
On right see building sign, take immediate right onto Church Street Extension.

From I-95 traveling south from Shoreline, New London, Norwich
I-95 south to exit 46/Long Wharf Drive.
Turn left off exit ramp onto Sargent Drive.
On right see building sign, take immediate right onto Church Street Extension.

From I-95 traveling north from Fairfield County and New York
I-95 north to exit 46/Long Wharf Drive.
Turn left off exit ramp.
At light turn left, pass under highway.
At light take left onto Sargent Drive. Pass IKEA.
On right see building sign, take immediate right onto Church Street Extension.

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