Ob/Gyn & Women’s Health Perspectives

An Update for Physicians from Cleveland Clinic’s Ob/Gyn & Women’s Health Institute

Exploring the feasibility of uterine transplantation

ALSO IN THIS ISSUE

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Dear Colleagues and Friends:

From the frontiers of infertility treatment to the vanguard of gynecologic cancer care, we have exciting and encouraging news to report in this issue of Cleveland Clinic’s Ob/Gyn & Women’s Health Perspectives.

Transplantation has become a viable option for patients in many dire medical situations, from end-stage renal and cardiac disease to leukemia and even devastating facial injuries, as evidenced by the pioneering face transplant surgery performed here at Cleveland Clinic. Now, in these pages, Cleveland Clinic Florida transplant surgeon Andreas Tzakis, MD, discusses the intriguing prospect of uterine transplantation to treat women with uterine factor infertility. There are daunting technical, ethical and procedural issues to be overcome, but we are part of the effort to evaluate uterine transplantation’s potential.

Elsewhere, you’ll learn from Cleveland Clinic Department of Gynecology’s Robert DeBernardo, MD, about hyperthermic intraperitoneal chemotherapy, or HIPEC, a promising technique that may extend life expectancy for women with gynecologic cancers. You’ll read about a Cleveland Clinic-developed protocol that has helped us reduce post-abdominal hysterectomy surgical site infections by 75 percent within one year. And you’ll hear from the Department of Obstetrics and Gynecology’s Karen Cooper, DO, about Be Well MomsSM, our unique, proactive program to tackle the problem of maternal obesity through education and counseling.

I’m proud of our efforts, which reflect Cleveland Clinic’s mission to develop and share the best in new knowledge and technology, and to constantly advance the care we provide our patients. In 2013, U.S. News & World Report ranked our gynecology program the nation’s third-best. It’s an honor we deeply appreciate, because it reflects the confidence of our medical colleagues. But it’s also a reminder that we must continue to strive for improvement. I hope you’ll follow our progress here and in the latest edition of our annual Outcomes book, available online at clevelandclinic.org/outcomes.

I look forward to continued collaboration with you, and welcome your questions and comments.

Sincerely,

Tommaso Falcone, MD
Professor & Chairman,
Department of Obstetrics and Gynecology
Chairman, Ob/Gyn & Women’s Health Institute
A solution to the problem of maternal obesity

Cleveland Clinic offers unique program

By Karen Cooper, DO

Today more than half the American women of reproductive age are overweight (BMI > 24.9) or obese (BMI > 29.9). Research shows that as BMI increases, so does the number of fetal tests, ultrasounds, prenatal visits and days in the hospital.

Maternal complications such as pre-eclampsia, hypertension and gestational diabetes increase with body mass index (BMI). So do neonatal complications such as open neural tube defects, cardiac defects, omphalocele, stillbirth and preterm birth.

The increase in complications and corresponding rise in healthcare costs are of particular concern in the new era of transparency about outcomes and hospital readmissions.

According to my colleague Jeffrey Chapa, MD, Head of Maternal-Fetal Medicine at Cleveland Clinic, “As healthcare providers, we spend a great deal of time diagnosing and treating complications during pregnancy but barely touch on important steps to prevent them. Patients frequently feel like there’s nothing they can do about their weight. But education, a preconception evaluation and nutritional guidance can be empowering — and can lead to better pregnancy outcomes.”

For these reasons, Cleveland Clinic has developed a unique maternal obesity weight management program, Be Well Moms®. Our program is designed to educate and counsel women before, during and after pregnancy about the benefits of achieving a healthy weight and the risks of not doing so — for them and their children.

A shared appointment setting

Women in Be Well Moms have been referred by their ob/gyns or primary healthcare providers or have self-referred. They attend shared appointments with me and a registered dietitian. During our 60-minute meetings, each patient can get answers to her questions and listen in as we address questions from others.

- **Before pregnancy.** Women learn how improving their health can help increase fertility and reduce the risks of miscarriage. A dietitian calculates each patient’s BMI and suggests weight loss tactics.

- **During pregnancy.** We discuss appropriate weight gain as well as the risks of gaining too much. Someone who has a BMI between 19 and 24.9 may be encouraged to gain between 25 and 35 pounds, while someone with a BMI of 30 or more may be encouraged to gain only 11 to 20 pounds.

- **After pregnancy.** If a new mother gained excessive weight during pregnancy, we identify dietary and exercise plans to help her lose it. Patients learn about controlling portions, reading food labels and making healthy family meals.

If your patients could benefit from weight management coaching before, during or after pregnancy, invite them to try Be Well Moms. Call 216.444.6601 for an appointment.

Dr. Cooper is an obesity medicine physician in the Department of Obstetrics and Gynecology at Cleveland Clinic. For more about the maternal obesity program, contact Dr. Cooper at cooperk2@ccf.org.
Exploring the feasibility of uterine transplantation

Can the procedure become a viable option for women with uterine infertility? Cleveland Clinic surgeons intend to find out.

Infertility is a major issue for thousands of women. For those with uterine factor infertility caused by a congenitally absent or removed uterus, traditional assisted-reproduction technologies may not be feasible. Although adoption and surrogacy provide opportunities for parenthood, both options pose logistical challenges and may not be acceptable due to personal, cultural or legal reasons.

Gynecologists, researchers and transplant surgeons are actively pursuing uterine transplantation as a potential method for helping women with uterine factor infertility start or build their families. Cleveland Clinic Florida transplant surgeon Andreas Tzakis, MD, joined one of the leading teams, which is conducting human clinical trials at the University of Gothenburg, Sweden. A forward-thinking transplant surgeon, he was motivated not by the opportunity to transplant a new organ, but by compassion for his patients.

“In my career, I have transplanted abdominal organs in young women who had no uterus. The thought crossed my mind that it would be wonderful if I could give them a uterus at the same time, so they could have their own babies,” he says.

Entering little-known territory

Uterine transplantation is not a new concept. In the past 20 years at least 11 attempts have been made outside the United States. The initial effort took place in Saudi Arabia in 2000. The recipient experienced two menstrual cycles post-transplant, but a vascular occlusion and necrosis prompted the organ’s removal after 99 days. The second uterine transplant, performed in Turkey in 2011, resulted in a brief clinical pregnancy 18 months later. The recipient miscarried after five weeks; the cause remains undetermined. The University of Gothenburg team performed the world’s third and fourth uterine transplants in September 2012, using two donors who provided organs to their respective daughters. The Swedish team subsequently has done an additional seven uterine transplants, for a total of nine, Dr. Tzakis reports, though the outcomes of those procedures had not been published as of late 2013.

The Swedish group is proceeding carefully after lengthy experimentation with small animals and baboons. For the last several years, Dr. Tzakis himself has been conducting research on swine as well as baboons. Although differences in physiology and reproductive anatomy make translating animal experience to human subjects difficult, the surgeons felt they had enough scientific evidence to proceed with clinical trials.

“We took information from each animal trial and patched it together. The amalgamation of this information was critical in the decision to proceed with a human trial,” says Dr. Tzakis.

Over a six-month period, the Swedish team performed transplants in nine women using uteri from related and unrelated living donors. Then they waited one year to ensure the new organ was successfully transplanted. The first embryo was recently implanted, and Tommaso Falcone, MD, Chairman of the Department of Obstetrics and Gynecology, and Cleveland Clinic Florida gynecologist Stephen Zimberg, MD, flew to Gothenburg with Dr. Tzakis to observe the surgery and meet the patients.

“Within the next year, we will know if these women can conceive and bear normal children,” says Dr. Tzakis.

An intriguing concept

Uterine transplantation represents a distinct departure from conventional models of transplantation. Unlike a liver or heart, the uterus is not a vital organ. In this respect, uterine transplantation is similar to hand, leg and face transplants, which are life-enhancing but not life-prolonging.

Yet uterine transplantation differs from these in one salient way: It is intended to be temporary — “ephemeral” is the term Dr. Tzakis prefers. Because its benefit ceases after childbearing is complete, the graft will be removed or allowed to be rejected after the child or children are born. This eliminates the need for lifelong immune suppression and associated medical problems.

Ethical considerations

Uterine transplantation raises many ethical issues. As an experimental process, its outcomes must undergo scientific scrutiny to ensure the safety of the transplant recipients as well as the children born of the process.
“Uterine transplantation could be an exciting option and very important for a couple who faces uterine factor infertility, yet much research remains to be done,” says Ruth Farrell, MD, a Cleveland Clinic ob/gyn and fellowship-trained bioethicist. “Researchers must not only examine the transplant procedure, but also determine outcomes during and after the pregnancy. Institutional review boards and bioethicists will have to work with researchers and physicians to ensure that adequate protections are in place both during and after the investigational phases of the procedure. Important topics, such as research on pregnant women, will be a part of these discussions.”

The issue of the ephemeral transplant also presents new and distinct challenges and, as such, must also be an important part of these deliberations.

“Typically, other transplanted organs are not removed unless they are dysfunctional,” she says. “The notion of removing the organ after childbearing raises issues such as, What additional risks would a woman be exposed to from the hysterectomy procedure? What if she would like to have more children? There may be many reasons why a woman may elect not to undergo additional surgery to have the uterus removed. These must be carefully considered by a transplant candidate and her healthcare team prior to initiating the procedure,” she adds. “This is just one of many issues that need to be addressed now, before research moves forward.”

**Other hurdles to overcome**

Ethical issues aside, there are many other hurdles that lie in the path to making uterine transplantation a viable option.

One is procedural. How would candidates be screened and chosen, and donors be identified, selected and protected in the short and long term?

Another issue is technical. Currently, removing a healthy uterus intact poses a challenge for surgeons. “The uterus must be taken out with care, because it must have sufficient vasculature to be reconnected. This process needs to be simplified,” says Dr. Tzakis. He and Dr. Zimberg intend to study new techniques for uterine removal.

Uterine transplantation is likely to be expensive, giving it little chance of being covered by private insurers. “Who would foot the bill for this procedure, which would be beyond the means of the average family?” says Dr. Tzakis.

Moreover, at a time when healthcare expenditures are being scrutinized, Dr. Farrell wonders whether Cleveland Clinic — or anyone else — could justify underwriting such an expensive procedure, when the funds could be used for primary and preventive healthcare needs.

An extensive analysis of the pros and cons of the procedure would be needed before uterine transplantation would be offered at Cleveland Clinic. Dr. Tzakis remains optimistic.

“If we can overcome the hurdles, we should be able to help these women bear their own children,” says Dr. Tzakis. ♦

Dr. Tzakis is a transplant surgeon in the Department of General Surgery at Cleveland Clinic and Cleveland Clinic Florida. He may be reached at 216.445.4793 or tzakisa@ccf.org.

### CME Activity:
**Ethical Dilemmas in the Practice of Obstetrics, Gynecology & Reproductive Medicine**

*Presented by Cleveland Clinic’s Ob/Gyn & Women’s Health Institute*

Medical professionals can discuss leading ethical issues and challenges in obstetrics and gynecology, maternal-fetal medicine, and reproductive endocrinology during a daylong activity on April 23, 2014, at Cleveland Clinic’s main campus.

“Ethical Dilemmas in the Practice of Obstetrics, Gynecology & Reproductive Medicine,” presented by Cleveland Clinic’s Ob/Gyn & Women’s Health Institute, will take place from 7:30 a.m. to 4 p.m.

Topics include maternal-fetal interventions, conscientious objection, perinatibility, advances in prenatal testing, uterine transplantation, oocyte cryopreservation, gestational surrogacy, and the clinical translation of innovative and experimental procedures into patient care.

The CME activity’s director is Ruth Farrell, MD, MA, of Cleveland Clinic’s Center for Ethics, Humanities and Spiritual Care. Co-directors are Tommaso Falcone, MD, Chairman of Cleveland Clinic’s Ob/Gyn & Women’s Health Institute, and Amanda Kalan, MD, an associate staff member in Cleveland Clinic’s Department of Obstetrics and Gynecology specializing in maternal-fetal medicine.

The activity has been approved for **AMA PRA Category 1 Credit™**.

To register, beginning January 2014, go to clevelandclinic.org/obgyn. For more information, contact Danielle Berry at berryd2@ccf.org or 216.445.2358.
Tackling surgical site infections
A multidisciplinary quality improvement project reduces gynecologic surgical site infections by 75 percent

To reduce surgical site infections (SSIs) following abdominal hysterectomy, Cleveland Clinic’s Department of Obstetrics and Gynecology initiated a project that employed a methodical process to systematically identify risk points potentially contributing to SSIs, then developed strategies to target modifiable risk points in order to reduce postoperative infection and develop institutionwide protocols to ensure sustained improvement. The goal was to reduce infections by 50 percent within one year. SSIs were actually reduced by 75 percent.

Risk points identified

Nineteen potential risk points were identified within the preoperative, intraoperative and postoperative surgical care episodes. Among them were:
- Bowel prep
- Preoperative patient education
- Glucose management in diabetics
- Hair clipping in the OR
- OR drape and prep
- Thermal regulation
- Postop wound care and dressing
- Perioperative antibiotic use
- Discharge education

Changes instituted

A multidisciplinary approach was used to develop standardized protocols designed to reduce risk. Successes included:
- Providing uniform instructions for preoperative skin care and showering
- Achieving antibiotic compliance
- Revising and improving skin care education materials to emphasize proper care of the incision site before and after surgery
- Instituting postop wound care education before surgery
- Reducing OR traffic to minimize introduction of infectious agents

- Standardizing OR prep and drape to eliminate variability of the sterile field
- Changing gloves at skin closure to avoid cross-contamination
- Achieving optimal control of blood glucose levels in diabetic patients
- Preventing hypothermia, since intraoperative hypothermia reduces peripheral blood circulation and increases risk of SSI

Results exceed expectations

Within 12 months, surgical site infections following abdominal hysterectomy were reduced by 75 percent. To maintain or improve this result, the team regularly:
- Compares outcomes with various surveillance data sources
- Measures compliance with new protocols
- Meets with residents, fellows, staff and nurses to reinforce protocols

So that others may benefit from our protocol, we have conducted a workshop for the American College of Surgeons National Surgical Quality Improvement Program and have plans for similar presentations at other national meetings.

For more information about the project to reduce surgical site infections, contact Mehdi Kebria, MD, an associate staff member in Cleveland Clinic’s Department of Obstetrics and Gynecology, at 216.445.7069 or kebriam@ccf.org.

Cleveland Clinic Florida Now an AAGL Fellowship Site

Young gynecologists interested in pursuing a two-year AAGL-accredited fellowship can now take advantage of the expertise available at Cleveland Clinic Florida. The first fellow started in July.

The fellowship’s goal is to provide training in both minimally invasive and robotic gynecologic surgeries, a dual emphasis that differentiates Cleveland Clinic Florida from other programs.

Cleveland Clinic Florida gynecologic surgeons utilize minimally invasive techniques in nearly all surgical cases, including the treatment of complex endometriosis, large fibroids and urogynecologic issues.

“Last year, we did only three abdominal hysterectomies. Everything else was done laparoscopically or vaginally,” says G. Willy Davila, MD, Chairman of Cleveland Clinic Florida’s Center for Gynecology, Urogynecology and Reconstructive Pelvic Surgery.

Virtually all procedures are done on an outpatient basis. “Even fibroid and prolapse patients go home the same day, and they do quite well,” says Dr. Davila.

In addition to perfecting minimally invasive techniques on complex gynecologic problems, Cleveland Clinic Florida offers training in robotic surgery, which continues to grow in popularity.

“Robotic surgery is useful for specific fibroids and prolapse procedures. Although it is often used in hysterectomies, it is unnecessary and adds dramatically to the expense,” says Dr. Davila.

For more information about the fellowships, contact Dr. Davila at 954.659.5559 or davilag@ccf.org.
Hyperthermic intraperitoneal chemotherapy (HIPEC) has been shown to extend the life expectancy of patients with peritoneal cancer of colorectal origin. The same technique is now showing promise for cancers of the peritoneal cavity arising from gynecologic cancers.

Robert DeBernardo, MD, a member of the Department of Gynecology who has been working with HIPEC for nearly three years, says the technique presents “a unique opportunity for women with gynecologic cancers.”

“We have found HIPEC to be effective for cancers of the ovary and fallopian tube, primary peritoneal cancer and, potentially, some advanced endometrial cancers,” he says. “Even with complete gross resection, microscopic disease is present and responds well to direct administration of chemotherapy in the abdomen. Heating these drugs during administration can augment their cytotoxicity.”

Changing the treatment paradigm
HIPEC is a welcome development in the treatment of a disease whose outcome has changed little in the past two decades. Surgical debulking followed by the introduction of intraperitoneal chemotherapy at normal temperature has been the most encouraging development, resulting in an improved survival of 1.5 years. Acceptance of the technique has been limited largely by its tolerability — an issue avoided by HIPEC, since patients are sedated for the procedure.

“HIPEC requires the patient be kept 90 minutes longer under anesthesia, but this allows us to expose the peritoneum to a very high concentrate of drug,” says Dr. DeBernardo.

Following the resection of visible disease, tubes are placed in the abdomen and the incision is closed. The drugs are heated and circulated under pressure, 45 minutes for the first drug and 45 minutes for the second drug. The tube is then removed, and the abdomen is irrigated and closed.

Altering the natural history of disease
Intraperitoneal chemotherapy extends life expectancy but does not necessarily cure gynecologic cancer. In some cases when the disease is eradicated in the abdomen, the women live longer and the cancer recurs elsewhere, usually in the lung, lymph nodes or liver.

Dr. DeBernardo also is working with colleagues in thoracic surgery to begin utilizing hyperthermic intrathoracic chemotherapy (HITEC) in patients with metastatic ovarian cancer involving the lung. HITEC follows the same procedure: removing the tumor and instilling heated chemotherapy directly in the chest cavity at the time of surgery. The technique has shown promise in the few women treated to date.

“We have high hopes HIPEC, and possibly HITEC, can extend remission in a meaningful way,” he says.

For more information about HIPEC and HITEC, contact Dr. DeBernardo at 216.444.7645 or debernr@ccf.org.
Resources for Physicians

Physician Directory. View our staff online at clevelandclinic.org/staff.

Same-Day Appointments. Cleveland Clinic offers same-day appointments to help your patients get the care they need, right away. Have your patients call our same-day appointment line, 216.444.CARE (2273) or 800.223.CARE (2273).

Track Your Patients’ Care Online. Establish a secure online DrConnect account for real-time information about your patients’ treatment at Cleveland Clinic at clevelandclinic.org/drconnect.

Critical Care Transport Worldwide. To arrange for a critical care transfer, call 216.448.7000 or 866.547.1467. Learn more at clevelandclinic.org/criticalcaretransport.

CME Opportunities: Live and Online. Visit ccfme.org to learn about the Cleveland Clinic Center for Continuing Education’s convenient, complimentary learning opportunities.

Outcomes Data. View Outcomes books at clevelandclinic.org/outcomes.

Clinical Trials. We offer thousands of clinical trials for qualifying patients. Visit clevelandclinic.org/clinicaltrials.

Executive Education. Learn about our Executive Visitors’ Program and two-week Samson Global Leadership Academy immersion program at clevelandclinic.org/executiveeducation.

About Cleveland Clinic

Cleveland Clinic is an integrated healthcare delivery system with local, national and international reach. At Cleveland Clinic, more than 3,000 physicians and researchers represent 120 medical specialties and subspecialties. We are a non-profit academic medical center with a main campus, eight community hospitals, more than 75 northern Ohio outpatient locations (including 16 full-service family health centers), Cleveland Clinic Florida, Cleveland Clinic Lou Ruvo Center for Brain Health in Las Vegas, Cleveland Clinic Canada, Sheikh Khalifa Medical City and Cleveland Clinic Abu Dhabi.

In 2013, Cleveland Clinic was ranked one of America’s top four hospitals in U.S. News & World Report’s annual “America’s Best Hospitals” survey. The survey ranks Cleveland Clinic among the nation’s top 10 hospitals in 14 specialty areas, and the top in heart care for the 19th consecutive year.