Single-Sperm Freezing Results in One Happy Family

p 8
CONTENTS

3 Study to Evaluate Decision-Making in New Prenatal Genetic Technologies
4 Role of Oxidative Cell Injury in Endometriosis Progression
5 First Documented Case of Endometriosis of the Vena Cava
6 Research Offers New Hope for Preserving Fertility in Cancer Patients
7 Cleveland Clinic’s IVF Lab Has New EmbryoScope
8 Single-Sperm Freezing Results in One Happy Family
10 Trophectoderm Biopsy for PGD
11 NextGenSM Home Sperm Banking Service Offers Reproductive Options
12 Fighting Cervical Cancer in the Developing World
14 Unique Ob/Gyn Residency Offers Tracking Into Subspecialties
16 Multidisciplinary Simulation Center Integrates Learning Opportunities
19 Clinical Trials
21 Selected Publications

Dear Colleagues and Friends:

We are pleased to present to you this the latest issue of Cleveland Clinic’s Ob/Gyn & Women’s Health Research Perspectives.

In the following pages, you will see a small sample of our innovative work and research efforts. We are making significant strides in the treatment of infertility; this issue offers a variety of articles addressing that topic. This edition will also give you an update on some exciting work dedicated to addressing cervical cancer internationally and grants and other research projects.

For information on how efficiently we care for our patients, please review the most recent edition of Cleveland Clinic’s Outcomes, available at clevelandclinic.org/outcomes.

Please feel free to contact us with suggestions and questions — we look forward to the collaborative possibilities those interactions may bring.

We hope that you find this publication valuable in your practice.

Sincerely,

Tommaso Falcone, MD
Professor & Chairman,
Department of Obstetrics and Gynecology
Chairman, Ob/Gyn & Women’s Health Institute

Matthew Barber, MD
Vice Chairman, Clinical Research
Ob/Gyn & Women’s Health Institute
Clinical genetics plays an increasingly important role in the delivery of routine and high-risk obstetrics. With more than 4 million women presenting for prenatal care in the U.S. annually, new genetic screening and diagnostic tests are becoming central tools to inform key decisions about pregnancy and antepartum management.

Informed decision-making is a key component of the translational pathway that brings scientific innovation to patient care. Thus, in order to realize the full potential of these new tools to assess fetal health, patients must be prepared to make decisions using those new tools; yet, those decisions must still be informed by and reflective of their own values and preferences. That is not an easy task. With increasing clinical demands and the rapid influx of new genetic tests, both patients and physicians struggle to surmount the challenges of the informed decision-making process.

The study is funded by an NIH KL2 Multidisciplinary Clinical Research Training Program of the Clinical and Translational Science Collaborative. Led by Ruth Farrell, MD, MA, the goal of the study is to identify patient-centered components to the decision-making process for first-trimester aneuploidy screening, a new approach to fetal risk assessment for chromosomal abnormalities. Using a combination of qualitative and quantitative methods, Dr. Farrell has identified pregnant patients’ baseline knowledge and attitudes about first-trimester screening, in addition to their patient-centered preferences for making an informed decision about the use of screening tools.

Dr. Farrell and the study team are currently using these data to inform the development of a series of educational tools to provide patients with the resources they need to make an informed decision, and physicians to facilitate patient-centered counseling regarding their genetic testing options. The goal of the work is to develop clinically responsive and evidence-based tools to assist pregnant women and obstetricians in the decision-making process with respect to using these new prenatal genetic technologies that will significantly improve access to and utilization of these new tools.

For additional information about this study, contact Dr. Farrell at 216.444.2615 or farrelr@ccf.org.
Study Suggests Possible Role of Oxidative Cell Injury in Endometriosis Progression

Oxidative stress has been proposed in many studies as a potential factor in the pathogenic and progressive advancement of endometriosis. Oxidative stress occurs when the production of reactive oxygen species (ROS) overwhelms the body’s natural ability to neutralize them with antioxidants. Endometriosis is considered a benign gynecological disease. However, in 40 percent of patients, it can become progressive and invasive.

The authors conducted a study to correlate and understand the relationship between oxidative stress and the progress of endometriosis by comparing the levels of ROS, total antioxidant capacity (TAC) and 8-OHdG in women with endometriosis compared with those same levels in women without endometriosis.

The study’s primary authors were Cleveland Clinic’s Luiz Carvalho, MD, Tommaso Falcone, MD, Charles Biscotti, MD, Rakesh Sharma, PhD, and Benjamin Nutter.

Peritoneal fluid was aspirated during laparoscopy, and endometriosis tissue was obtained by biopsy during laparoscopic surgery.

Eleven women with endometriosis were divided into two groups: stage I/II (n=6) and stage III/IV (n=5). Seven fertile women without endometriosis at laparoscopy were used as a control group. To be included in the study, all women had to be of reproductive age, had reported pelvic pain and had visually confirmed endometriosis. Women with a history of smoking, signs of past or present pelvic inflammatory disease, and autoimmune disease were excluded for this analysis.

Levels of ROS were measured in the peritoneal fluid using luminol as the probe by chemiluminescence assay. TAC was assessed using an antioxidant assay kit. Immunohistochemical staining was performed on paraffin blocks to assess DNA damage by the 8-OHdG assay.

As a result of oxidative stress, patients with advanced-stage endometriosis (stage III/IV) had significantly higher DNA damage, as demonstrated by increased staining of 8-OHdG, than did stage I/II and control patients.

Dr. Falcone is Professor and Chairman of the Ob/Gyn & Women’s Health Institute. Physicians may reach him at 216.444.1758 or falconet@ccf.org.
In the recent article “Post-menopausal Endometriosis With Inferior Vena Cava Invasion Requiring Surgical Management,”* Rebecca Flyckt, MD, and Tommaso Falcone, MD, from Cleveland Clinic’s Ob/Gyn & Women’s Health Institute describe a never-before-reported case of recurrent endometriosis that had invaded a patient’s inferior vena cava. Although symptomatic recurrent endometriosis can respond to treatments such as progestins, oral contraceptive pills, danazol, GnRH agonists, and aromatase inhibitors, surgical management is sometimes required.

In this case, a postmenopausal patient had already undergone total abdominal hysterectomy and bilateral salpingo-oophorectomy more than a decade before the heart issue presented itself. Her recurrence of endometriosis was large (more than 8 cm) and appeared to encase the aorta and inferior vena cava. After the endometriosis failed to respond to a trial of aromatase inhibitors, the decision was made to proceed with surgery to resect what had become an even larger mass that also involved the ureter.

A combined effort between Cleveland Clinic’s vascular surgeons, urologists and gynecologists yielded a good result. After a 19-day postoperative hospitalization complicated resulting from ileus and ascites complications due to venous outflow obstruction and lymphatic leak, the patient is now symptom-free. The final pathology report of the excised segment of vena cava showed involvement of endometriosis in the vein wall.

No previous case reports have described endometriosis occluding and invading the inferior vena cava.◆

Dr. Flyckt is with the Ob/Gyn & Women’s Health Institute. Physicians may reach her at 216.444.6601 or flycktr@ccf.org.

Research Offers New Hope for Preserving Fertility in Cancer Patients

Infertility is a significant complication of cancer treatment because many treatments can substantially damage or destroy a young woman’s reproductive system. Understanding that this is often a major concern, Cleveland Clinic has given considerable attention to the long-term reproductive health of women of childbearing age undergoing cancer treatment.

In an effort to offer new hope for preserving fertility, Nina Desai, PhD, HCLD, Director of IVF and Clinical Research, and colleagues have developed a mouse model for maturing enzymatically isolated preantral follicles suspended three-dimensionally in a tyramine-based hyaluronan (HA) hydrogel culture system.

Whereas a conventional culture system limits the growth of the follicle, forcing granulosa cells to attach to the surface of the culture and abandon the oocyte, the HA culture system more closely mimics the follicles’ natural growth conditions without disrupting the complex interactions between somatic cell components and the oocyte that are necessary for cytoplasmic and nuclear maturation.

Dr. Desai and her team tested several encapsulation methods and HA gel concentrations and examined the ability of HA-embedded follicles to mature in vitro and produce mature metaphase II oocytes.

The investigators were able to develop mature eggs with apparently normal meiotic spindles, suggesting the eggs could go on to normal fertilization and embryonic development, which will be the second stage of the research.

The study will be published in the journal *Reproductive Biology and Endocrinology*.

For more information about this study, contact Cleveland Clinic’s Fertility Center at 216.839.3150
Cleveland Clinic’s IVF lab at the Beachwood Family Health & Surgery Center is now one of only 10 labs in the United States and the only lab in Ohio with the EmbryoScope™ (Unisense® FertiliTech) used to continuously monitor embryo development from conception to time of transfer. The device will open up a whole new area in understanding embryo development, allowing staff to identify new grading criteria for embryo selection.

This high-tech device allows the incubation of up to 72 embryos at a time — 12 from each of six patients. A built-in camera provides automated and continuous time-lapse imaging of fertilized oocytes without disturbing their environment.

Because data suggest that the timing of variables such as pronuclear formation, syngamy, early cleavage, compaction and cavitation are indicators of an embryo’s developmental potential, this device will provide embryologists the ability to evaluate these variables at many more time points. As the IVF lab and physicians gather more information about the early development of the embryos and the resulting pregnancies, they can add to the grading criteria for selecting embryos with the best implantation potential.

A novel benefit for patients is that they can receive a CD showing the cleavage of all their embryos prior to implantation and witness the development of their baby from the very beginning.

For more information about this procedure, contact Cleveland Clinic’s Fertility Center at 216.839.3150.
In situations where both partners experience fertility issues, special attention and teamwork are necessary to achieve pregnancy. In the case of one couple recently treated at Cleveland Clinic, male fertility issues called for a novel solution to a problem that has challenged investigators for almost 15 years.

With severe male factor infertility, the number of sperm available may be very limited. The laboratory needs to be able to reliably isolate and freeze the few sperm that can be found. One sperm is all that the fertility experts had to work with in the case of Jason and Jennifer Schiraldi, and fortunately for the couple, one sperm is all it took to achieve conception.

This successful outcome resulted from the collaborative efforts of In Vitro Fertilization Lab Director Nina Desai, PhD, and Edmund Sabanegh, MD, Director of the Center for Male Fertility at the Glickman Urological & Kidney Institute.

After a standard course of testing to address fertility concerns, it was discovered that this couple was experiencing issues on both sides of the equation: Jason Schiraldi was diagnosed with azoospermia, and Jennifer Schiraldi had a diminished capacity to produce eggs.
Dr. Sabanegh recommended the standard course of investigation for a patient with this condition who wishes to pursue parenthood.

“We conducted blood tests and ultrasounds, which pointed to severe testicular failure,” Dr. Sabanegh says. “Jason was experiencing an issue we see in less than 10 percent of men who come into a fertility practice.”

Dr. Sabanegh elected to perform a delicate microsurgical testicular biopsy on Jason Schiraldi with the hope of extracting enough sperm for the couple to proceed with an IVF cycle.

“We were trying to find a small area that could be producing sperm,” Dr. Sabanegh says.

“I usually conduct between 15 and 50 biopsies in each patient, which takes between one and four hours. In almost 80 percent of those biopsies, at least some viable sperm are found.”

Dr. Desai’s lab was responsible for assessing the tissue samples for the presence of sperm and ultimately freezing the tissue for Jennifer’s treatment cycle.

Very few sperm were present. The laboratory elected to freeze a single motile sperm it had found and isolated after extensive screening. The hope was that if all the tissue were screened, more viable sperm would be found.

“In some ways, the procedure is akin to looking for a needle in a haystack,” says Dr. Sabanegh. “In this case, it was.”

The Single-Sperm Freezing process starts with the very careful microsurgical biopsy of the testicles by an andrologist to identify small areas of potential sperm production. In the IVF laboratory, a sample is screened at 300 times magnification for the presence of sperm. Living sperm are identified and retrieved with a glass needle. After incubation with a cryoprotectant, sperm are ready to be frozen.

With the aid of a microscope, the sperm are moved with a fine glass needle to the freezing device. The sperm is sequestered in one microliter or less of fluid and then placed on a plastic capillary tube with a preformed gutter. The capillary tube is then placed into another straw and sealed. The straw is then slowly cooled before being stored in liquid nitrogen.

On the day of Jennifer’s egg retrieval, after another three to four hours of searching by three technicians, no living sperm could be found.

“We made the decision to use the single sperm that had been initially found and frozen after the intricate search undertaken in the lab, to inject one oocyte,” says Dr. Desai. “Jennifer’s remaining eggs had to be frozen due to lack of sperm.”

Fortunately for the couple, one sperm was all it took. The egg was successfully fertilized and developed normally. After three days, the embryo was transferred to Jennifer’s uterus. Sixteen days later, Jennifer and Jason learned that they were to become parents. Daughter Kenley was born on April 20, 2011, after a normal pregnancy.

According to Dr. Sabanegh, a small minority of practicing urologists conduct microsurgical testicular biopsies and work extensively with severe male factor infertility.

“Not many places in the country have been able to form the very close partnership that we have at Cleveland Clinic between the Glickman Urological & Kidney Institute and Dr. Desai’s laboratory at the Ob/Gyn & Women’s Health Institute,” says Dr. Sabanegh. “Our success is realized through a seamless collaboration that puts our patients first.”

To learn more about this procedure, contact Cleveland Clinic’s In Vitro Fertilization Laboratory at 216.839.3150.
Trophectoderm biopsy for PGD offers greater diagnostic confidence, increases potential for successful pregnancy outcome

Cleveland Clinic’s Fertility Center now provides patients access to a cutting-edge technique for genetic screening of patient embryos, which offers several advantages over traditional PGD techniques that remove a single cell on Day 3. This powerful new technique, known as trophectoderm biopsy, allows the removal of multiple cells at the blastocyst stage. Embryos can be screened for inherited genetic disorders as well as chromosomal abnormalities. By selecting only normal embryos are selected for transfer, the patient’s opportunity for a healthy pregnancy and baby is increased.

Trophectoderm biopsy is performed on Day 5, at the 16- to 32-cell blastocyst stage when the embryo has the highest implant potential. A laser is used to open the zona pellucida and excise five or six cells from the trophectoderm as it begins to herniate. The inner cell mass is unaffected. The cells are analyzed using a highly valid and rapid microarray technology offered by Genesis Genetics Institute.

This technology examines 24 chromosomes for abnormalities by comparing the sample against a known normal control. A computer-generated chromosome map is produced for each embryo sample. Embryos found to be abnormal are discarded, and only the chromosomally normal embryos are implanted. The screen is completed within 24 hours, allowing patients to have fresh embryo transfers in the same IVF cycle.

Because trophectoderm biopsy looks at multiple cells at a point when the embryo has shown developmental potential, it offers greater diagnostic confidence and a higher likelihood of a successful implantation and a healthy pregnancy outcome. The technique is especially powerful for patients of advanced maternal age who have a high rate of aneuploid embryos, patients with naturally recurring miscarriages and unsuccessful IVF cycles, patients with unexplained infertility, and those concerned about passing on known inherited genetic mutations.

For more information about this procedure, contact Cleveland Clinic’s Fertility Center at 216.839.3150.
All of Cleveland Clinic’s endeavors focus on putting the patient first. In keeping with this long-established tradition, the Reproduction Lab recognizes that many patients may view sperm donation as a personal and private activity.

As a result, Cleveland Clinic’s Andrology Lab and Reproductive Tissue Bank has established the new and novel NextGen Home Sperm Banking Service. Individuals opting for this service will receive a specially designed donor kit that is delivered with instructions. Home donation alleviates the anxiety that may accompany donations in a clinic donation room. This program is ideal for men with cancer or underlying subfertility, pre-vasectomy patients who may want to cryopreserve in advance of their vasectomy, men with a desire to ensure potential future fertility and military personnel going on long-term deployment.

Those interested in exploring this service may call 1.866.922.6546 (866.9BANKIN) Monday through Friday between 7:30 a.m. and 4 p.m. ET to speak with a specialist who will explain the process in detail. He or she will acquire the necessary information and accept a credit card payment for the service during the conversation. The specialist with then contact Path-Tec, a company specializing in sample collection, and request they send a sample-collection kit. This kit contains collection materials, complete instructions and some additional forms that require signatures. Once the sample is collected, it is returned to the Andrology Lab. Tests will be conducted and results reported quickly.

Cleveland Clinic offers two means of donating sperm, both of which require referral from a physician and completion of the appropriate paperwork. In addition to home sperm banking, a donor can visit the Andrology Laboratory and Reproductive Tissue Bank in the Glickman Urological & Kidney Institute on Cleveland Clinic’s main campus. Following completion of the appropriate paperwork, the donor will complete the donation process in private in a room designed for that purpose.◆

This service requires a physician referral. For more information about the kit, call 1.866.922.6546.
In the past year, Preventive Oncology International (POI) has moved closer to fulfilling its primary goal of bringing cervical cancer screening to women in developing countries, where cervical cancer is the leading cause of death from cancer in young women. Since POI was established 15 years ago with the support of Cleveland Clinic’s Section of Gynecologic Oncology, we have tested a wide range of screening technologies. We have incorporated these technologies to develop procedures that are accurate, easy-to-use and cost-effective and applicable to areas where the healthcare infrastructure is limited or nonexistent. Based on our studies conducted in China, Mexico and Peru, we have concluded that if one hopes to initiate large-scale screening programs that can truly make a significant difference in reducing the prevalence of worldwide cervical cancer, the most feasible options will be self-sampling-based.

We recently completed a 10,000-woman randomized trial in China and demonstrated conclusively that a self-collected sample is as sensitive as a physician-obtained specimen for the detection of high-grade precancer and cancer. We clearly demonstrated the high-risk HPV assay to be the critical element, not the specific design of the collection device as we had previously thought would be the case. In addition, we demonstrated for the first time that the type of assay that would be required was possible with a very high-throughput, low-cost-per-case testing platform. Our findings were reported in the August 2011 epub of the International Journal of Cancer and were published in print in the April 15, 2012, issue.

These findings have set the stage for extensive worldwide cervical cancer screening programs and have shifted our focus from evaluating screening technologies to developing and implementing preventive healthcare models that will allow the technology to reach the people most in need. However, testing new technologies will continue to be part of our research; for example, we are now evaluating a new HPV assay using gene sequencing that will fit nicely into our algorithms. We continue run trials on our inexpensive self-collection kit for women called “Just for Me,” which is currently being produced in China.

Implementing Community-Based Healthcare
In our Chinese Cancer Prevention Study (CHICAPS), begun in November 2011, and PERCAPS (a similar study we began earlier in Peru), we are applying the concepts used in community-based participatory research to develop collaborative
relationships with community leaders for the design and implementation of models for preventive healthcare. We believe that many types of preventive healthcare can be performed by the communities, with the medical community becoming involved once the positive at-risk population has been identified. Having community members involved in the design and administration of a screening program will allow greater recruitment, fuller participation and minimal loss to follow-up.

In April 2012, we completed two pilot studies (1,000 women screened) and will soon move into the application phase of the study, screening 9,000 women for cervical cancer over seven to 10 days using our community-based model. This trial will “stress” our model and ideally will accurately assess the community’s ability to conduct its own screening program. Study investigators will evaluate the program to determine the percentage of the population reached by the screening protocol and the percentage of HPV screen-positive women who return for evaluation and treatment. Based on the results, we will create a community-based manual for cervical cancer screening that the Chinese government can use to implement programs, especially throughout rural China.

In Peru, we completed similar community-based pilot studies in Manchay, a large squatter community outside Lima, and in Iquitos, the largest city in the Loreto region, as well as five villages along the Amazon River. We have moved from a medical infrastructure model to a community-based model in which the community will primarily manage the program. We are currently seeking funding to screen the 126,000 women, aged 30 - 50 in 2,600 villages in the Loreto region. In addition, we plan to evaluate cold-coagulation technology as a possible replacement for cryotherapy in Third-World screening programs.

**Expanding Cancer Screening**

Receiving China’s highest honor awarded to a foreigner, the Chinese Friendship Award, in 2010, I hope will give us the opportunity to explore new directions and include other cancers in our work. Awards such as this one are important if they lead to an expansion of the work we are doing. We are currently seeking funding to establish the Preventive Oncology Institute of China, which will initially focus on cervical, lung, breast, colorectal, prostate and liver cancers.

**Publications and Additional Educational Opportunities**

The new centralized PCR-based technology was a focus of the December 2011 issue of the *American Journal of Clinical Pathology* and our epidemiological data in a *Lancet Oncology* collaborative paper. Through the POI Research and Education Fund, established within Cleveland Clinic’s Department of Obstetrics and Gynecology by POI, we currently have fellows and medical students from the U.S. and China working on our projects.

We have accomplished a great deal at the POI sites in the past year and look forward to continued progress. ♦

Dr. Belinson is Professor of Surgery at Cleveland Clinic’s Lerner College of Medicine and President of Preventive Oncology International Inc. For additional information, visit poiinc.org or call 216.312.3663.
Unlike other residency training programs in the nation, Cleveland Clinic’s Ob/Gyn residency training program allows residents the flexibility to design their own program. This new program began recruiting its first class last fall. It is expected that those residents will finish the program in June 2016.

In this “trainee-centered” program, residents have the option to track into a curriculum specifically designed to provide more extensive experience in the gynecologic subspecialties. This flexible training concept also allows residents to spend more time within the chosen subspecialty areas of interest, thereby gaining increased proficiency in advanced procedures and becoming more active in the surgical management of patients and complex decision-making.

**Flexibility Leads to Greater Focus**

Most obstetrics and gynecology residency programs in the U.S. have a rigid and fixed curriculum that focuses largely on training in obstetrics and less focus on gynecologic training. The major strength of Cleveland Clinic’s program lies in the breadth and depth of exposure to gynecologic surgical training while maintaining core training in obstetrics.

By the end of the first year, residents may choose to concentrate their training in general Ob/Gyn or choose to concentrate their training in one of the following subspecialty tracks:

- Gynecologic oncology including breast surgery
- Female pelvic medicine and reconstructive surgery
- Reproductive endocrinology and infertility
The five themes within each obstetrics and gynecology track are:

• Primary and Preventive Ambulatory Health
• Obstetrics
• Gynecology
• Reproductive Endocrinology
• Gynecologic Oncology

There are several rotations within each theme, some of which are core for specified levels of the program. The remainder of rotations contributes to a wide menu of options from which residents select according to their needs.

Twenty resident positions (five per level) are available for this four-year program. In addition to this core training, which residents need to pass their boards, residents also have the opportunity to gain significant experience and a deeper understanding of gynecologic surgical training and issues in women’s health that physicians deal with daily.

Experiences Provided Throughout Cleveland Clinic

Most training will take place at Cleveland Clinic’s main campus. Residents also train at Hillcrest and Fairview hospitals, both of which are Cleveland Clinic health system hospitals that provide obstetrics care. General and subspecialty operative gynecology are also performed in these locations. Additionally:

• Fairview Hospital features a level III perinatal center, a level III NICU and a level II trauma center.
• Hillcrest Hospital features a level III NICU and level II trauma center.

In each year of training, residents rotate through the Hillcrest and Fairview hospitals’ high-risk labor and delivery service and the maternal-fetal medicine clinics.

One morning per week is departmental-protected conference time for faculty and trainees. The first Wednesday of the month is morbidity and mortality conference, the second Wednesday is the journal club, the third and fifth Wednesdays are Grand Rounds, and the fourth Wednesday is administrative time.

Resident-protected education time occurs every Wednesday morning following departmental-protected times. During these sessions, various didactics, small-group activities, simulations and hands-on activities are conducted.

Patient rounds are scheduled at various times depending on the service and clinical volumes. Continuity clinics take place at Cleveland Clinic’s main campus and regional sites, and all are precepted by full-time Ob/Gyn generalist faculty members who have training and interest in outpatient clinical teaching.

Educational activities are monitored through semiannual program reviews, rotation-by-rotation specific feedback, program surveys, and attendance at conferences, rounds and journal clubs. Residents also have other collaborative learning and research opportunities made available to them.

For more information, please contact Pat Wolf, Ob/Gyn Residency Program Manager, at 216.444.4884 or wolfp@ccf.org.

Applications for Cleveland Clinic’s Ob/Gyn residency are accepted through the Electronic Residency Application Service (ERAS) at aamc.org/students/medstudents/eras.
Imagine a state-of-the-art — and science — patient simulation center only steps from the front door of one of the nation’s leading medical institutions. A center with what could be a functioning operating room, teleconferencing facilities and roomy mock examining rooms where future physicians hone their skills.

Cleveland Clinic recently completed such a center in the Stanley Shalom Zielony Center for Nursing Education. In a building that once housed a health museum, the Center for Multidisciplinary Simulation occupies space that includes technology gifts from major medical supply providers and a $200,000 “patient” that can react to and with medical procedures and drugs.

J. Eric Jelovsek, MD, is the medical director of the center. He says that the new center demonstrates Cleveland Clinic’s multidisciplinary focus.

“The organization of the center is consistent with Cleveland Clinic’s model of being a multidisciplinary practice,” he says. “We are not prevented by our business model, with its multidisciplinary approach, from working together — there’s no barrier there to overcome.”

Real-World Experience

When a simulation is conducted in the new facility, one of the staff of four simulation lab managers employed by the center ensures that the simulation details are just right for each purpose. Extensive planning goes into each scenario, and debriefing sessions take place after each one.

The centerpiece of the facility is a complete operating room. Most of the devices provided by donors are put to use in this full-size, fully equipped facility that contains gases, monitors, booms and other relevant equipment.

Lying on the operating table is a sim patient that can respond to various inputs in the operating room, from oxygen to some medications. Real surgeries can be practiced by medical staff, right down to taking a blanket from a blanket warmer for the patient.

Down the hall from the OR is a large room similar to an emergency room, with multiple beds, monitors and other devices, including blood pressure cuffs. Built into the ceiling and walls are video...
cameras that can observe every procedure being conducted in the room; a sophisticated sound system can record every word. One wall is devoted to a glass-paneled control and observation room, where instructors or other evaluators can observe students from a slightly elevated view. Computers provide constant feedback on how the students are doing, and those observing can provide instructions through the sound system.

“If one of the observers notices something that could be done a little bit better from their perspective,” says Dr. Jelovsek, “they can directly address it by providing feedback at that moment.

The debriefing process is aided by the sophisticated recording system, which documents every move and sound in the operating or examination room. The system is part of the extensive control room, supported by a massive computer server located down the hall from the action in its own large room.

“In the debriefing room we can replay the entire treatment scenario and review a procedure, without judgment. The process is designed to educate, not find fault,” he says. “The entire sim might take 20 minutes, but the debriefing process can take one to two hours.”

Procedures can also be shared remotely in the debriefing area. Cleveland Clinic facilities in other states and other countries can share information and standardize enterprisewide training through this novel means.
Down the hall from the OR are two critical care rooms, each of which can accommodate three patients. These are also equipped as if a real patient were about to step into the room for care — with real booms and examination tables.

**Real Devices Provide Real Learning**
The medical device community has embraced this learning laboratory and has reached out to support it extensively.

In-kind donations or financial support have been provided by InterMetro, GE Healthcare, STERIS Corporation, Siemens Healthcare and Welch Allyn. CareFusion donated a Pyxis® Anesthesia System 3500, and Laerdal came forward with a SimMom™.

**Have Sim Tools, Will Travel**
While the center provides real medical equipment and places to use it, it also is responsible for in situ simulations across Cleveland Clinic’s system.

“In situ simulations are great for a number of reasons,” Dr. Jelovsek says. “People don’t have to travel. The simulation can be tailored to be very specific to that work environment. And, they can provide a quality assurance aspect when our team arrives and has to use equipment that is on-site.”

Dr. Jelovsek says the quality assurance facet came into play recently when the team went out to train a department and discovered that the software on a defibrillator had not been fully updated.

“When the team was out conducting a simulation that involved running a code, they learned that the old ACLS software had not been updated,” he said. “That ‘aha’ moment allowed Cleveland Clinic staff to look for other units across the system and update them too.

“Aside from serving a quality assurance function, personnel get refreshed on rare events too.”

In situ simulations conducted by the mobile team have included training at Cleveland Clinic’s newly opened Special Delivery Unit, at the emergency department and at obstetrical events at regional hospital locations — again integrating Cleveland Clinic experience throughout a hospital system that covers most of Northeast Ohio. The team also conducts simulations for the Critical Care Transport Team, right inside ambulances and aircraft.

The Multidisciplinary Simulation Center also is responsible for several sim sites throughout Cleveland Clinic, including nursing and surgical sim sites, and a pediatric difficult-airway center.

**Not Acting, But Reacting**
Dr. Jelovsek points out that simulation training is important in that it helps create an emotional component that is lacking in merely manipulating equipment in a lab.

“Aside from maintaining the quality that accrediting organizations require,” he says, “it is important to show that we can simulate and account for the psychological distress that could set in during a simulation.

“It takes about five seconds to suspend the disbelief that this is not real,” he says. “They realize they’re performing the procedure, just like on a real patient, since the tools react to inputs. Participants begin to sweat a little, and their pulse rates go up.

“The experience is great at demonstrating that emotional component. And it helps participants understand how that component can impact performance.”

For more information about Cleveland Clinic’s Center for Multidisciplinary Simulation, go to simcenter.clevelandclinic.org.

The debriefing room allows the simulation team to gather to review the procedure, either in the room or remotely.
Cleveland Clinic has a robust research program in gynecologic cancers. For more information, call 216.445.8090.

**BENIGN TRIALS**

**Title:** Prevention of Catheter-Associated Urinary Tract Infection in Incontinence and Reconstructive Pelvic Surgery (PRECAUTION)  
IRB: 10-125  
Treatment: Reconstructive Pelvic Surgery  
Status: Open  
Principal Name: Ellen Solomon, MD  
Research Line: 216.445.8090

**Title:** Assessment of Voiding After Sling (AVAS): A Randomized Trial of Two Methods of Post-operative Catheter Management After Midurethral Sling for Female Stress Urinary Incontinence  
IRB: 11-082  
Treatment: Stress Incontinence  
Status: Open  
Principal Name: Elena Tunitsky-Bitton, MD  
Research Line: 216.445.8090

**Title:** Vaginal Uphold Hysteropexy and Laparoscopic Sacral Hysteropexy for the Treatment of Uterovaginal Pelvic Organ Prolapse: A Parallel Cohort Study (VaULT)  
IRB: 11-409  
Treatment: Pelvic Organ Prolapse  
Status: Open  
Principal Name: Matthew Barber, MD  
Research Line: 216.445.8090

**Title:** Refractory Overactive Bladder: Sacral NEuromodulation v. BoTulinum Toxin Assessment (ROSETTA)  
IRB: 12-003  
Treatment: Urge Incontinence  
Status: Open  
Principal Name: Sandip Vasavada, MD  
Research Line: 216.445.8090

**Title:** Laparoscopy vs. Robotic Surgery for Endometriosis (LAROSE): A Prospective Randomized Controlled Trial  
IRB: 12-173  
Treatment: Infertility  
Status: Open  
Principal Name: Enrique Soto, MD  
Research Line: 216.445.8090

**ONCOLOGY TRIALS**

**Title:** GOG0076HH A Limited Access Phase I/II Trial of Paclitaxel, Cisplatin and CTEP-Supplied Agent ABT-888 (Veliparib) (IND#77840,NSC#737664) in the Treatment of Advanced, Persistent or Recurrent Carcinoma of the Cervix  
IRB: CC00095  
Treatment: Cervical Cancer  
Status: Open  
Principal Name: Peter Rose, MD  
Research Line: 216.445.8090

**Title:** GOG0131H A Phase II Evaluation of ixabepilone (IND #59699, NSC #710428) in the Treatment of Recurrent or Persistent Leiomyosarcoma of the Uterus  
IRB: CC00059  
Treatment: Uterine Cancer  
Status: Open  
Principal Name: Peter Rose, MD  
Research Line: 216.445.8090

**Title:** GOG0186G A Randomized Phase II Evaluation of Everolimus (RAD001) Plus Bevacizumab vs. Oral Placebo Plus Bevacizumab in the Treatment of Recurrent or Persistent Epithelial Ovarian, Fallopian Tube or Primary Peritoneal Cancer  
IRB: CC00127  
Treatment: Ovarian, Fallopian Tube or Peritoneal Cancer  
Status: Open  
Principal Name: Peter Rose, MD  
Research Line: 216.445.8090

**Title:** GOG0186I A Randomized Phase II Evaluation of Single-Agent Bevacizumab (IND #7921) (NSC #704865) and Combination Bevacizumab With Fosfotabulin Tromethamine (CA4P) (NSC #752293) in the Treatment of Recurrent or Persistent Epithelial Ovarian, Fallopian Tube or Primary Peritoneal Carcinoma  
IRB: CC00061  
Treatment: Ovarian, Fallopian Tube or Peritoneal Cancer  
Status: Open  
Principal Name: Peter Rose, MD  
Research Line: 216.445.8090

**Title:** GOG0187 Phase II Study of Paclitaxel for Ovarian Stromal Tumors as Second-Line Therapy  
IRB: CC444  
Treatment: Ovarian Cancer  
Status: Open  
Principal Name: Peter Rose, MD  
Research Line: 216.445.8090
Title: GOG0213 A Randomized Controlled Clinical Trial of Platinum-Combination, Sequence-Dependent Chemotherapy and Secondary Cytoreductive Surgery in Platinum-Sensitive, Recurrent Ovarian and Peritoneal Primary Cancer  
IRB: CC444  
Treatment: Ovarian and Peritoneal Cancer  
Status: Open  
Principal Name: Peter Rose, MD  
Research Line: 216.445.8090

Title: GOG0250 A Randomized Phase III Evaluation of Docetaxel (NSC#628503) and Gemcitabine (NSC#613327) Plus G-CSF With Bevacizumab (NSC#704865, IND#7921) vs. Docetaxel (NSC#628503) and Gemcitabine (NSC#613327) Plus G-CSF With Placebo in the Treatment of Recurrent or Advanced Leiomyosarcoma of the Uterus  
IRB: CC852  
Treatment: Uterine Cancer  
Status: Open  
Principal Name: Peter Rose, MD  
Research Line: 216.445.8090

Title: GOG0258 A Randomized Phase III Trial of Cisplatin and Tumor Volume-Directed Irradiation Followed by Carboplatin and Paclitaxel vs. Carboplatin and Paclitaxel for Optimally Debulked, Advanced Endometrial Cancer  
IRB: CC735  
Treatment: Endometrial Cancer  
Status: Open  
Principal Name: Peter Rose, MD  
Research Line: 216.445.8090

Title: GOG0260 A Phase II Evaluation of Elesclomol Sodium and Weekly Paclitaxel in the Treatment of Recurrent or Persistent Platinum Resistant Ovarian, Fallopian Tube or Primary Peritoneal Cancer  
IRB: CC0126  
Treatment: Ovarian, Fallopian Tube or Peritoneal Cancer  
Status: Open  
Principal Name: Peter Rose, MD  
Research Line: 216.445.8090

Title: GOG0261 A Randomized Phase II Trial of Paclitaxel Plus Carboplatin vs. Ifosfamide Plus Paclitaxel in Chemotherapy-Naive Sex Cord-Stromal Tumors of the Ovary  
IRB: CC906  
Treatment: Ovarian Cancer  
Status: Open  
Principal Name: Peter Rose, MD  
Research Line: 216.445.8090

Title: GOG0273 Chemotherapy Toxicity in Elderly Women With Ovarian, Primary Peritoneal, or Fallopian Tube Cancer  
IRB: CC00204  
Treatment: Ovarian, Peritoneal or Fallopian Tube Cancer  
Status: Open  
Principal Name: Peter Rose, MD  
Research Line: 216.445.8090

Title: GOG0274 A Phase III Trial of Adjuvant Chemotherapy Following Chemoradiation as Primary Treatment for Locally Advanced Cervical Cancer Compared to Chemoradiation Alone: The OUTBACK Trial (ANZGOG 0902/GOG-0274/RTOG 1174)  
IRB: CC00194  
Treatment: Cervical Cancer  
Status: Open  
Principal Name: Peter Rose, MD  
Research Line: 216.445.8090

Title: GOG9923 A Phase I Study of Carboplatin/Paclitaxel/and CTEP-Supplied Bevacizumab (NSC #704865, IND #7921) and CTEP-Supplied ABT-888 (NSC #737664 IND # 77840) in Newly Diagnosed Patients With Previously Untreated Epithelial Ovarian, Fallopian Tube or Primary Peritoneal Cancer  
IRB: CC853  
Treatment: Epithelial, Fallopian Tube or Cervical Cancer  
Status: Open  
Principal Name: Peter Rose, MD  
Research Line: 216.445.8090
Journal Articles


Rose PG, Monk BJ, Provencher D, Hartney J, Legenne P, Lane S. An open-label, single-arm phase II study of intravenous weekly (days 1 and 8) topotecan in combination with carboplatin (day 1) every 21 days as second-line therapy in patients with platinum-sensitive relapsed ovarian cancer. *Gynecol Oncol*. 2011 Jan;121(1):38-42.


Infertility Publication Highlights


Books, Whole


Resources for Physicians

Referring Physician Center and Hotline
Cleveland Clinic’s Referring Physician Center has established a 24/7 hotline — 855.REFER.123 (855.733.3712) — to streamline access to our array of medical services. Contact the Referring Physician Hotline for information on our clinical specialties and services, to schedule and confirm patient appointments, for assistance in resolving service-related issues, and to connect with Cleveland Clinic specialists.

Physician Directory
View all Cleveland Clinic staff online at clevelandclinic.org/staff.

Track Your Patient’s Care Online
DrConnect is a secure online service providing real-time information about the treatment your patient receives at Cleveland Clinic. Establish a DrConnect account at clevelandclinic.org/drconnect.

Critical Care Transport Worldwide
Cleveland Clinic’s critical care transport teams and fleet of vehicles are available to serve patients across the globe.

• To arrange for a critical care transfer, please call 216.448.7000 or toll-free 866.547.1467 (see also clevelandclinic.org/criticalcaretransport).
• For STEMI (ST elevated myocardial infarction), acute stroke, ICH (intracerebral hemorrhage), SAH (subarachnoid hemorrhage) or aortic syndrome transfers, call 877.379.CODE (2633)

Outcomes Data
View clinical Outcomes books from all Cleveland Clinic institutes at clevelandclinic.org/outcomes.

Clinical Trials
At any given time, we offer thousands of clinical trials for qualifying patients. Visit clevelandclinic.org/clinicaltrials.

CME Opportunities: Live and Online
The Cleveland Clinic Center for Continuing Education’s website offers convenient, complimentary learning opportunities. Visit ccfcme.org to learn more and use Cleveland Clinic’s myCME portal (available from the site) to manage your CME credits.

Executive Education
Cleveland Clinic has two education programs for healthcare executive leaders — the Executive Visitors’ Program and the two-week Samson Global Leadership Academy immersion program. Visit clevelandclinic.org/executiveeducation.

24/7 References

Referring Physicians Hotline
855.REFER.123 (855.733.3712)

Hospital Transfers
800.553.5056

On the Web at
clevelandclinic.org/refer123

Stay Connected to Cleveland Clinic

About Cleveland Clinic
Cleveland Clinic is an integrated healthcare delivery system with local, national and international reach. At Cleveland Clinic, 2,800 physicians represent 120 medical specialties and subspecialties. We are a main campus, 18 family health centers, eight community hospitals, Cleveland Clinic Florida, the Cleveland Clinic Lou Ruvo Center for Brain Health in Las Vegas, Cleveland Clinic Canada, Sheikh Khalifa Medical City, and Cleveland Clinic Abu Dhabi.

In 2011, 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 13 specialty areas, and among the top 2 in four of those areas.
Subscribe to *Infertility eNews*

The latest information on infertility — delivered to your inbox!

*Infertility eNews* is an online publication that includes timely and practical health information from Cleveland Clinic. Designed for primary care physicians as well as obstetricians and gynecologists, *Infertility eNews* will serve as a clinical resource for your practice by featuring our institutional perspective on stories making medical headlines, and highlighting new services and technology that impact clinical care.

Subscribe at [clevelandclinic.org/ObGynNews](http://clevelandclinic.org/ObGynNews).

Join Cleveland Clinic’s Fertility Center Facebook Group 📡

Harness the social networking power of Facebook to share information about infertility.

- Go to [clevelandclinic.org/FertilityFacebook](http://clevelandclinic.org/FertilityFacebook)
- Click on “Ask to Join Group”

Visit our group page often to interact with our physicians, nurses and embryologists as they share the latest information on infertility diagnoses, treatments and procedures. Engage with patients facing the same challenges. Feel free to invite others with an interest in this topic to join the discussion.