

Ob/Gyn & Women's Health Institute

**2020 Year in Review**

## MESSAGE FROM THE CHAIR

Dear Colleagues,

I am pleased to share the Cleveland Clinic Ob/Gyn & Women's Health Institute's 2020 Year in Review, which highlights our continued progress in all aspects of women's health.

2020 has been a year of unprecedented change. The evolving COVID-19 pandemic has had a profound impact on clinical care, education and research. After initially postponing nonemergent procedures in March, we worked diligently to return surgical volumes close to pre-COVID-19 levels in October. Now, we face uncertainty once again as COVID-19 cases and hospitalizations are increasing dramatically. In women's health, we are particularly concerned with the complex nature of COVID-19 in pregnancy and the transition to virtual visits amid the pandemic; we explore both topics in this issue.

Despite these challenges, we continue our pursuit of excellence in women's health. In 2020, we expanded our team of subspecialists, including Edward Chien, MD, MBA, Chair, Department of Obstetrics and Gynecology; Laura Detti, MD, Chair, Department of Subspecialty Care for Women's Health; and Amy Park, MD, Section Head, Female Pelvic Medicine & Reconstructive Surgery. We delivered the second baby from our deceased donor uterine transplant program. We received our second endowed chair in gynecologic oncology. We continued to work with leaders across our region to improve pregnancy outcomes. Our fetal surgery program is thriving and has completed 15 open fetal surgeries through the end of October. And there's so much more!

The year of change is not over for us. In November, I was named Cleveland Clinic's Chief of Staff. I will continue to care for patients, and women's health will always remain a priority. However, this new position means that my time as Institute Chair must come to an end. I am so proud of what we've been able to accomplish in my short time as Chair, and look forward to seeing our work continue to evolve. It is a true privilege to work alongside such talented, committed and compassionate caregivers.

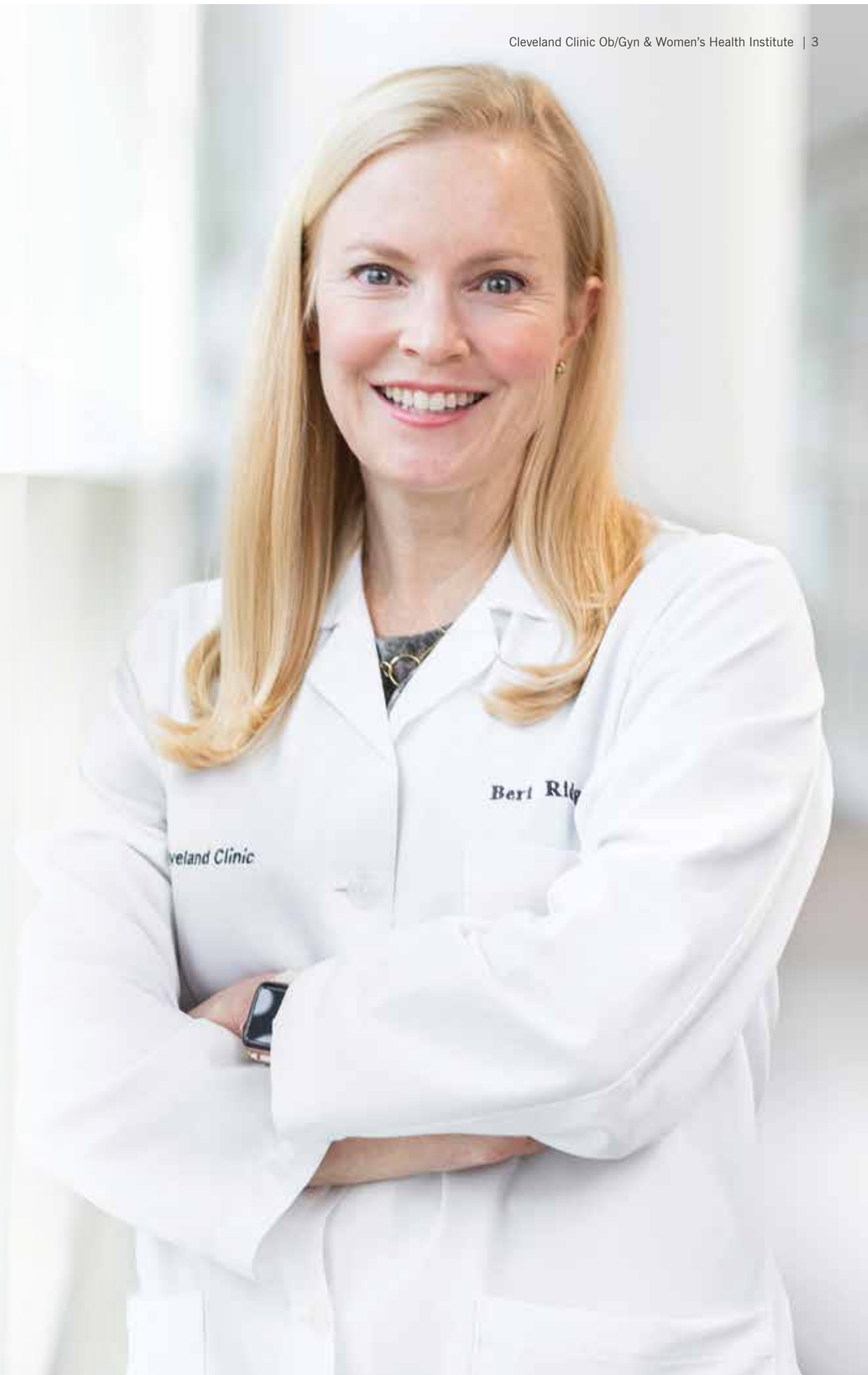
I applaud our team's exceptional work in patient care, research and education, and invite you to read more about it in these pages. I encourage you to reach out with questions and feedback.

Sincerely,

**Beri Ridgeway, MD**

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On the cover: Following hysterotomy, the fetal surgery team, led by Darrell Cass, MD, exposes the head, torso and right arm.





The mother and fetus are monitored closely using an arterial catheter in the mother, and ongoing ultrasonography and echocardiography for the fetus. Ultrasound is also used to identify the fetus's position and the location of the placenta to guide the uterine incision.

## First Fetal Surgery Cases Set the Course for a Full Spectrum of Intrauterine Therapies

A great start and a look ahead

When pediatric and fetal surgeon Darrell Cass, MD, joined Cleveland Clinic in October 2017, his mission was to establish Cleveland Clinic as a global leader in fetal surgery. In only a few short years, Dr. Cass has made great strides toward this goal. Thanks to carefully timed and expert operations, fetuses that would have died can be saved and expected to develop normally, and fetuses with other anomalies can be repaired antenatally to minimize their risk for lifelong disability.

### The beginning of an era

A multidisciplinary team of Cleveland Clinic surgeons, led by Dr. Cass, performed the institution's first fetal surgery in February 2019: a complex in utero repair of a neural tube defect in a nearly 23-week-old fetus. Historically, myelomeningocele (MMC) repair was completed postnatally, limiting the opportunity to prevent neurologic loss.

In December 2019, Dr. Cass and team successfully established an airway in a partially delivered fetus with a large trachea-obstructing neck mass, enabling safe birth and subsequent mass removal. The procedure, known as EXIT (ex-utero intrapartum treatment)-to-airway, takes advantage of uteroplacental blood flow and maternal-fetal gas exchange while the fetus's trachea is secured. This minimizes the risk of life-threatening asphyxia or hypoxia at birth due to airway obstruction. In this

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first case at Cleveland Clinic, the fetus had a giant neck mass at the anterior aspect of the trachea that was compressing the trachea and esophagus, which posed a risk of death and need for risky emergency airway interventions immediately after birth. Instead, the airway was safely secured, allowing successful resection of the neck mass the day after delivery.

In June 2020, the Cleveland Clinic team successfully performed an EXIT-to-resection procedure on a partially delivered hydroptic fetus with a large, right-sided lung mass. In the procedure, Dr. Cass exteriorized the lung mass, enabling safe birth and subsequent removal of the tumor. Although it was the first time Dr. Cass performed the operation at Cleveland Clinic, he has unique experience with this intervention, having performed it successfully 18 times previously. In total, Cleveland Clinic's team has completed 15 open fetal surgeries through the end of October.

#### Expert team

Cleveland Clinic Children's Fetal Care Center is a collaborative team of highly skilled and compassionate healthcare professionals who offer leading-edge techniques and interventions with a family-centered approach. Dr. Cass has high praise for the team and the outcomes they achieve.

"Each of these complex procedures requires the involvement of more than a dozen physicians and nurses who specialize in pediatric surgery, maternal-fetal medicine, fetal cardiology, pediatric and obstetric anesthesiology, and neonatal intensive care. Additional specialists, like pediatric neurosurgeons for MMC, may be required depending on the procedure. At Cleveland Clinic, our patients benefit from a growing team of top subspecialists in their fields who work together seamlessly to help the mother and the fetus as it transitions from the in utero environment to life as a neonate," Dr. Cass says.

The fetal surgery team includes maternal-fetal medicine specialists Amanda Kalan, MD, and Jeff Chapa, MD; pediatric cardiologists Francine Erenberg, MD, Rukmini Komarlu, MD, and Holly Nadorlik, DO; obstetric and pediatric anesthesiologists McCallum Hoyt, MD, MBA, Tara Hata, MD, and Yeal Dahan, MD; pediatric otolaryngologist Samantha Anne, MD; and pediatric neurosurgeons Violette Recinos, MD, and the late Kaine Onwuzulike, MD, PhD.

#### Future plans

Dr. Cass expects the program's volume and diversity of cases to continue to grow.

"I'm very pleased with the progress our program has made," he says. "The complexity that we've been dealing with is already high. We're going to do more and different types of procedures, and work to expand our outreach beyond the local region to our campuses in Florida and then to our international campuses. Giancarlo Mari, MD, a maternal-fetal medicine specialist with international expertise in fetoscopy and fetal treatment of twin-twin transfusion syndrome, has recently joined our Fetal Care Center team. He brings complementary expertise that will help take our program to the next level. In partnership with Dr. Mari and the entire fetal surgery team, our goal is to become one of the world's leading fetal care programs. I'm very excited about the future," Dr. Cass concludes.

In this instance, the fetus was delivered with the mass exteriorized through an open chest, and then ventilated. The lobectomy was completed following delivery.



## Second Live Birth From a Deceased Donor Transplant at Cleveland Clinic

A closer look at the transplant procedure and fertility treatments provided to a patient with MRKH syndrome

For the second time in Cleveland Clinic's clinical trial, a patient has given birth after receiving a transplanted uterus from a deceased donor. The first birth from this program was in June 2019.

"This is one of very few live births from a deceased donor — every one of them is a landmark that confirms feasibility," says transplant surgeon Andreas Tzakis, MD, who has spearheaded Cleveland Clinic's efforts to develop and advance the procedure. "This birth is further proof of principle that deceased donor transplants can lead to joyous outcomes for our patients."

This patient had Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome — a congenital abnormality in which Müllerian agenesis or hypoplasia leads to variable uterine development and partial absence of the vagina. Patients with MRKH are not usually diagnosed until mid- to late puberty, and as they have functioning ovaries, tend to develop as expected until they reach an age by which menstruation is expected to begin. Incidence of MRKH is estimated at 1 in 4,500 women.<sup>1</sup>

"It can be a devastating diagnosis," says Stephanie Ricci, MD, a gynecologic oncologist on the transplant team. "Often there is no external sign, so the news that they cannot carry a child comes as a great shock. I can't tell you how much joy pregnancy and birth bring to these women."

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These births are the culmination of years of research and preparation by Cleveland Clinic's multidisciplinary uterine transplant team.

## The Multi-Step Path to Parenthood



### Candidates start the screening process.

- Cleveland Clinic's transplant study will include 10 women.
- All candidates must be 21-39 years old and have UFI.
- The transplant team must unanimously approve each candidate.



### Evaluations are in-depth.

- Teams of doctors, surgeons, psychologists, social workers and bioethicists evaluate each candidate.
- Candidates face in vitro fertilization and then several surgeries, and must understand the study's risks and limitations as well as other options.



### A search for donors follows.

- The organ procurement agency searches for a donor 18-40 years old.
- The donor's uterus must be healthy.
- The next-of kin must sign an informed consent.



### In vitro fertilization (IVF) begins.

- After selection for the study, the woman's ovaries are stimulated to produce multiple eggs.
- Her eggs are removed and fertilized with sperm in the IVF lab.
- 6-10 embryos are selected and frozen.



### Transplant takes place within 6-8 hours.

- The woman starts anti-rejection drugs to prepare for transplant.
- The donor's uterus is removed along with its blood supply.
- The uterus is transplanted into the woman's pelvis. The donor's blood vessels are connected to hers.



### Once the uterus heals, the embryos are transferred.

- A few months after transplant, the woman starts having periods.
- 12 months after transplant, her uterus fully heals.
- Her embryos are thawed and implanted one at a time.
- The goal is 1-2 pregnancies.



### Motherhood at last.

- The baby is delivered by C-section.
- After 1-2 babies, the woman has a hysterectomy to remove the transplanted uterus.
- After hysterectomy, the anti-rejection drugs are stopped to reduce long-term exposure to the medications.



### Each pregnancy is closely monitored.

- A high-risk obstetrics team monitors the woman throughout pregnancy and delivery.
- She takes anti-rejection drugs throughout pregnancy.
- She needs monthly cervical biopsies to check for organ rejection.

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### The process

Patients who are selected for the clinical trial must first undergo in vitro fertilization (IVF) and cryopreservation of at least six embryos harvested by a team of IVF specialists. That is followed by a wait for a matching deceased donor (a woman of reproductive age who has previously given birth), the transplant surgery, immunosuppression and infection prophylaxis, embryo transfer, cesarean delivery and eventual hysterectomy to remove the graft after one or two pregnancies.

"After uterus transplantation, we follow patients closely in the clinic — weekly at first, and then monthly. Patients generally begin to menstruate that first postoperative month, as was the case with this patient. With no sign of rejection after about six months, we begin preparations for embryo transfer," Dr. Ricci explains.

"We retrieved 25 eggs from the patient prior to transplant. Of those, several were successfully fertilized and all but one developed normally to the blastocyst stage and were cryopreserved," reports Elliott Richards, MD, Director of Reproductive Endocrinology and Infertility Research and co-investigator in Cleveland Clinic's uterus transplant clinical trial.

"Following transplant, the patient's menstrual cycle was evident within the first month, and her transplanted uterus responded beautifully to the hormones we prescribed to prepare the endometrial lining. Her embryo likewise looked to be of excellent quality. The process of embryo transfer was really no different than for any other IVF patient here."

"As in any embryo transfer, we first perform a 'mock transfer' to ensure that we can pass a tiny catheter through the cervix into the uterine cavity. Then the embryo is loaded onto an identical catheter and, under ultrasound guidance, the embryo is gently introduced into the upper portion of the uterine cavity. For this patient, we had easy visibility of the cervix and were able to transfer the embryo without difficulty. She then had a blood test 12 days later that confirmed pregnancy."

"In this case, the patient developed hypertension," says Uma Perni, MD, a maternal-fetal medicine specialist who follows patients in the trial once pregnancy is achieved. "We delivered just prior to full term in order to avoid complications such as preeclampsia. The baby was quite healthy. He was taken to the NICU, and, after about one week, was discharged home without complications."

### Reference:

<sup>1</sup> Herlin M, Bjørn AM, Rasmussen M, Trolle B, Petersen MB. Prevalence and patient characteristics of Mayer-Rokitansky-Küster-Hauser syndrome: a nationwide registry-based study. *Hum Reprod.* 2016 Oct;31(10):2384-2390.

## Management of Pregnant Women With COVID-19 Infection Proves Complex

Preterm delivery and other complications of COVID-19 in pregnancy

Emerging infections can have an important impact on pregnant women and their unborn children, leading to an increased risk of complications. SARS-CoV-2 is no exception, and as the COVID-19 pandemic has evolved, data have emerged indicating that pregnant women with the virus are 5.4x more likely to be hospitalized, 1.5x more likely to be admitted to the intensive care unit (ICU) and 1.7x more likely to receive mechanical ventilation than women who are not pregnant.<sup>1</sup>

### Pregnancy management during the pandemic

Symptomatic nonpregnant women with COVID-19 reported higher frequencies of headache, muscle aches, fever, chills and diarrhea than symptomatic pregnant women with the virus.<sup>1</sup> Additionally, the severity of some symptoms appears to be higher in pregnant women with COVID-19 than in the nonpregnant cohort, as 31.5% of pregnant women with the virus were hospitalized compared with 5.8% of nonpregnant women.

“Management of pregnant women with COVID-19 is complicated, as they have increased risk of complications, such as ICU admission and intubation, in part due to physiologic, anatomic and immunologic changes in pregnancy,” says Oluwatosin Goje, MD, an Ob/Gyn and fellowship-trained reproductive infectious diseases specialist. “This is in line with our experience in prior public health crises, like the 2009 H1N1 influenza virus pandemic and the Zika virus outbreak.”

### Preterm delivery and other complications of COVID-19 in pregnancy

Emerging studies also point to a higher risk of preterm birth and prematurity in pregnant women with COVID-19, with incidence of 28%.<sup>2</sup> More recently, a retrospective analysis of a much smaller cohort of patients from rural France reported preterm delivery in 36% of patients.<sup>3</sup>

“Prematurity is one of the complications you’ll find when pregnant women become very sick with COVID-19,” says Dr. Goje. Among pregnancies resulting in live births, pregnant women with symptomatic COVID-19 infection were about 3x more likely to deliver preterm; specifically, preterm delivery was reported for 23.1% of symptomatic women and 8.0% of asymptomatic women.<sup>4</sup>

That point was brought home by the recent case of a woman in her early 30s and in her late second trimester, who presented to Cleveland Clinic’s emergency department for weakness, myalgia, subjective fever and a dry cough. Like her husband, she tested positive for SARS-CoV-2. She was admitted to the hospital due to the severity of symptoms and managed per protocol; she received betamethasone and magnesium sulfate after the possibility of early delivery was discussed in multidisciplinary meetings. When her disease progressed and she went into respiratory failure, she was intubated and her infant delivered by cesarean section at 26w2d. Unfortunately, the child died of complications of extreme prematurity. Thanks to the excellent care of maternal-fetal medicine experts at Cleveland Clinic, the mother recovered and was discharged home seven days after the procedure.

Says Dr. Goje, “COVID-19 is novel and we are still gathering information about optimal management of women who are pregnant and positive for COVID-19.

It is well-known in the MFM literature, however, that delivery can help in treating mothers in the setting of worsening respiratory failure, and with intermittent hypoxia, fetal well-being is at risk in utero.”

### References:

- 1 Ellington S, Strid P, Tong VT, et al. Characteristics of women of reproductive age with laboratory-confirmed SARS-CoV-2 Infection by Pregnancy Status — January 22–June 7, 2020. *Morbidity and Mortality Weekly Report* (MMWR). 2020 Jun;69(25):769-775.
- 2 Trippella G, Ciarcia M, Ferrari M, et al. COVID-19 in pregnant women and neonates: a systematic review of the literature with quality assessment of the studies. *Pathogens*. 2020 Jun;9(6):485.
- 3 Vivanti AJ, Mattern J, Vauloup-Fellous C, et al. Retrospective description of pregnant women infected with severe acute respiratory syndrome coronavirus 2, France. *Emerg Infect Dis*. 2020 Sep;26(9):2069-2076.
- 4 Delahoy, MJ, Whitaker M, O’Halloran A. Characteristics and maternal and birth outcomes of hospitalized pregnant women with laboratory-confirmed COVID-19 — COVID-NET, 13 states, March 1–August 22, 2020. *Morbidity and Mortality Weekly Report* (MMWR). 2020 Sept 25;69(38):1347-1354.



## Leadership in the Time of COVID-19: Building Strong Teams for Optimal Agility

A conversation with Beri Ridgeway, MD

The COVID-19 pandemic has brought unprecedented challenges. We sat down with Beri Ridgeway, MD, Chair of Cleveland Clinic's Ob/Gyn & Women's Health Institute (WHI), to discuss reactivation, telehealth, caregiver safety and agility in leadership amid the pandemic.

**Q: What processes are in place to help Cleveland Clinic leaders understand the evolving COVID-19 pandemic, as well as the needs of our patients and caregivers in this time of crisis?**

**A:** In terms of surgical operations, our first task as a team was to work with the government to limit our surgeries to those that were essential. Prior to the pandemic, we performed about 800 cases each day across Northeast Ohio. During the shutdown, we did roughly 200 cases per day — emergent cases that could not be deferred. During this time, we redeployed many of our caregivers and repurposed equipment from our ambulatory surgery centers in preparation for the anticipated surge in COVID-19 cases.

When Ohio's curve appeared to flatten in May, we worked with the government to reopen as quickly as possible, as a slew of people with very serious diagnoses had been deferring care. Our reactivation strategy was a phased approach based on preoperative testing of all pre-surgical patients. We reactivated in early May and have seen increasing cases each week — we're probably at about 90% of our pre-COVID-19 levels.

**Q: In the span of 6 weeks, total Cleveland Clinic outpatient visits went from 2% remote (virtual or phone) to 75% remote. What kinds of issues arose as we made this transition, and how were they addressed to ensure the highest-quality care?**

**A:** In Ob/Gyn specifically, we had already been conducting a small percentage of low-risk prenatal visits via a remote platform. We expanded this platform and also effectively offered these visits for infertility consults, preconception counseling, post-partum checks, birth control, preoperative counseling, and follow-up for laparoscopic surgery.

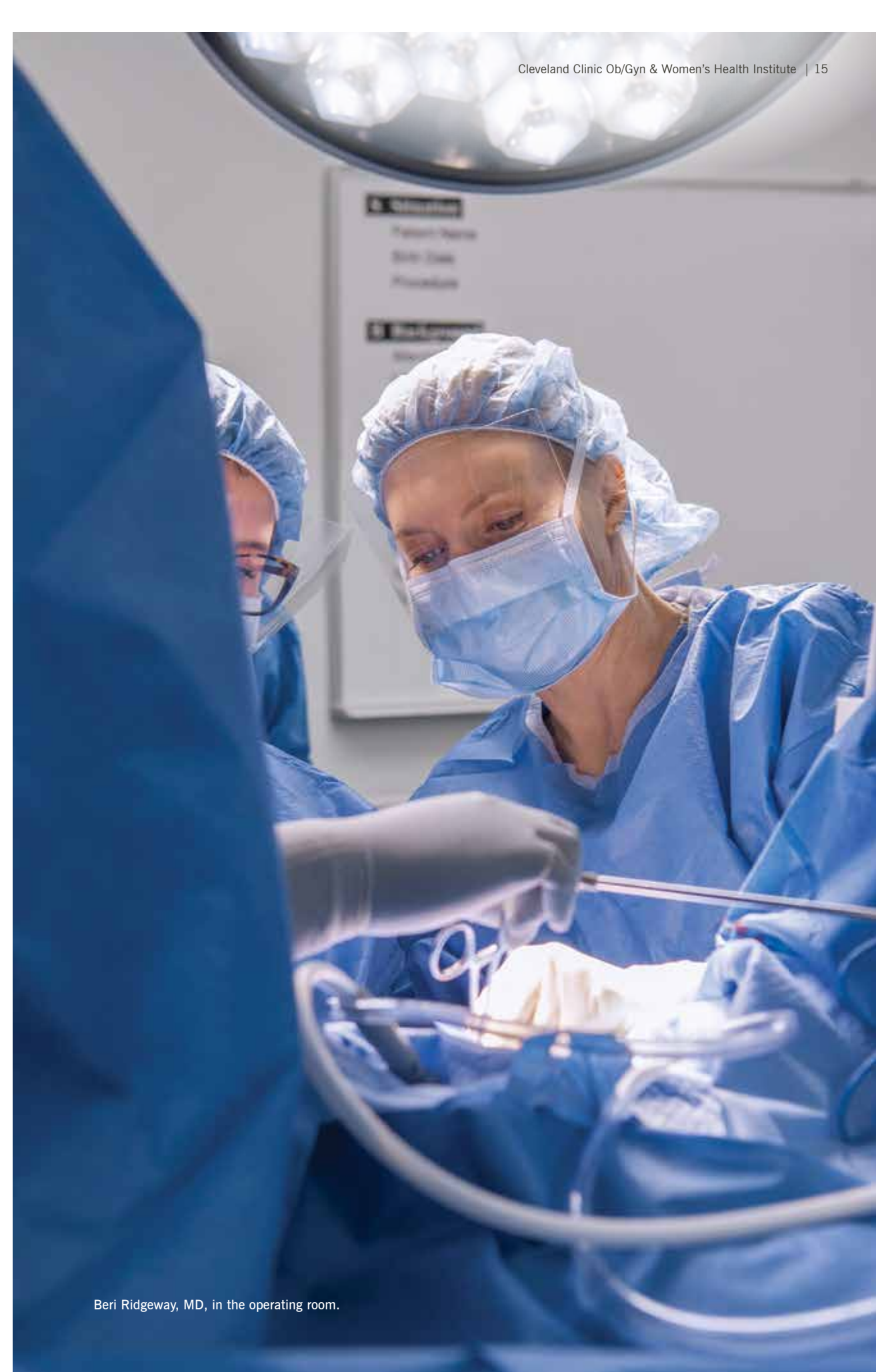
Some patients really love telehealth, while it was more challenging for others and not how they'd like to receive care going forward. It is nice to have options for our patients as we continue to emphasize how important it is to seek medical care. We remain concerned that there will be public health issues related to deferred diagnosis and care for patients with cancer or heart disease, and we're looking at strategies to minimize these effects.

**Q: How has your leadership changed since the beginning of the pandemic?**

**A:** Prior to the pandemic, we had the luxury of time. I feel like we had the opportunity to review and revise communications or presentations many times over. Now, we just don't have that kind of time. As leaders, we've had to stay agile, make the best decisions with the limited amount of data available and then move forward with the plan to iterate once new data are available.

I think it's really impossible to over-communicate right now. That's an elusive — yet worthwhile — goal I feel as though I'm constantly working toward.

Finally, I rely heavily on others. I rely on my colleagues in leadership, and I rely on the leadership structure we've implemented and the fabulous caregivers in the WHI. We've created fantastic teams, and as a consequence of that, we're able to come to the best possible solutions.



Beri Ridgeway, MD, in the operating room.





## Extended Use of Pegylated Liposomal Doxorubicin Offers Clinical Benefit in Women With Recurrent Ovarian Cancer

Treatment may allow patients more time with less toxicity

A 45-year-old patient with stage IIIC high-grade serous ovarian cancer underwent a hysterectomy, bilateral salpingo-oophorectomy, omentectomy and debulking before receiving adjuvant chemotherapy with six cycles of intravenous cisplatin and cyclophosphamide.<sup>1</sup> A second-look surgery revealed microscopic residual disease. She was treated with four cycles of intraperitoneal cisplatin followed by etoposide.

After an extended disease-free interval, biopsy revealed disease recurrence in the liver and spleen, for which she received two years of oral etoposide. Further evidence of progression was noted nearly 16 years from the original diagnosis. The patient was started on pegylated liposomal doxorubicin (PLD) 40mg/m<sup>2</sup>. The PLD was well tolerated, and the patient remained on it for more than 100 cycles, resulting in a cumulative dose of 4600mg/m<sup>2</sup>. More than 25 years from the original diagnosis, the patient's Eastern Cooperative Oncology Group performance status remained 1. Her disease was stable for nine years.

### Limited treatment options

Patients with recurrent epithelial ovarian cancer, especially when their tumors become resistant to platinum chemotherapy, have limited treatment options, and their disease is rarely curable, according to Robert DeBernardo, MD, Laura J. Fogarty Endowed Chair in Women's Health for Uterine Cancer Research and Director of the Peritoneal Surface Malignancy Program at Cleveland Clinic's Ob/Gyn & Women's Health Institute.

"At this point in their treatment course, we tend to look for chemotherapy drugs with clinical benefit,

acceptable toxicity and durable response," Dr. DeBernardo says. "In our practice, we noticed that a subset of patients taking PLD responded well and were able to stay on it for many months or years."

With this insight, Dr. DeBernardo and his team sought to assess oncologic outcomes and toxicity in patients with recurrent ovarian cancer treated with PLD (N = 69) who had more than seven cycles of PLD.<sup>2</sup> "This retrospective study was the next logical step," Dr. DeBernardo explains.

"Among this cohort of women with recurrent ovarian cancer who had clinical benefit after six cycles of PLD, we found that continued use is both well tolerated and effective," says Laura Chambers, DO. "Nearly 60% of patients saw clinical benefit from extended PLD treatment, and about 32% of patients developed toxicities, most of them dermatologic."

### PLD versus native doxorubicin

Native doxorubicin was approved by the U.S. Food and Drug Administration in 1964 and is used widely in oncology. Although it has been used for years, the drug has a significant and potentially life-threatening toxicity profile. In PLD, the liposomal encapsulation reduces the incidence of acute and chronic toxicities, including myelosuppression, dermatitis, stomatitis and cardiotoxicity.

"While doxorubicin is associated with dose-dependent cardiotoxicity, the liposomal encapsulation makes the treatment less toxic to the heart. Our data support that the risk of cardiac complications is low with extended use of PLD. While these data are derived from a relatively small cohort of patients, we believe

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that these results support that women with recurrent ovarian cancer who have experienced a response to PLD may safely stay on it indefinitely, with acceptable toxicity," Dr. Chambers says.

Despite the overall lower toxicity profile, cases of oral squamous cell carcinoma have been reported in women receiving long-term PLD.<sup>3</sup> "In this cohort, we identified four patients who were diagnosed with early-stage oral cancers (a rate of 5.8%), and one of these women was a smoker. As a result, we recommend conducting an oropharyngeal exam as part of routine chemotherapy evaluations to ensure that there are no lesions that need to be evaluated or biopsied. Overall, our results indicate that if a patient is responding to PLD therapy and is tolerating it well, we can keep them on PLD indefinitely — until their cancer progresses," says Dr. DeBernardo.

#### References:

<sup>1</sup> Pendlebury A, DeBernardo R, Rose PG. Long-term use of pegylated liposomal doxorubicin to a cumulative dose of 4600 mg/m<sup>2</sup> in recurrent ovarian cancer. *Anticancer Drugs*. 2017 Aug;28(7):815-817.

<sup>2</sup> Chambers LM, Pendlebury A, Rose PG, Yao M, DeBernardo R. Efficacy and toxicity of prolonged pegylated liposomal doxorubicin use in women with recurrent epithelial ovarian cancer. *Gynecol Oncol*. 2020 Aug;158(2):309-315.

<sup>3</sup> Rose PG, Fu F, Chambers LM, et al. Incidence of squamous cell carcinomas of the head and neck following prolonged pegylated liposomal doxorubicin. *Anticancer Drugs*. 2020 Aug; 31(7):747-750.

## First Documented Use of Buccal Mucosa Graft in Rectoneovaginal Fistula Repair in Transgender Woman

**Durable repair with good function and no symptoms of recurrence at six months**

A 64-year-old transgender woman with recurrent rectoneovaginal fistula (RnVF) presented for care following penile skin inversion neovaginoplasty at an outside institution. The index surgery had been complicated by an intraoperative rectal injury, which was repaired in two layers. One week following the neovaginoplasty, the patient was allowed to dilate her neovagina. She developed an RnVF, which was initially managed with a diverting loop ileostomy. When the ileostomy was reversed three months later, the RnVF symptoms returned immediately.

#### An uncommon complication

Transgender women with RnVF present with a set of symptoms that are clinically similar to neovaginal fistula in natal women, namely drainage of feces and or passage of flatus from the neovagina. RnVF is an uncommon but morbid complication following neovaginoplasty. Despite its relative rarity, neovaginal fistula is a known complication of each of the five steps in male-to-female gender affirmation surgery: orchiectomy, disassembly of the penis, creation of a neovaginal cavity, urethral meatus construction, neoclitoris construction and creation of labia. The most significant risk factor is intraoperative rectal perforation, which occurred in this patient's index surgery.

A multidisciplinary team, including colorectal surgery, reconstructive urology and urogynecology, proceeded with laparoscopic diverting loop ileostomy

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and rectoneovaginal exam under anesthesia. The exam revealed a 2- to 3-cm fistula at the cephalad neovagina, roughly 6 cm proximal to the anorectal ring. The providers developed a surgical plan and took the patient into surgery for fistula repair using a buccal mucosa graft (BMG) three months later.

Options for repair include fistulectomy with primary closure, local advancement flaps, pedicled flaps and/or free flaps. The surgical team chose to use an autologous BMG because, similar to native vaginal tissue, oral mucosa is thick, nonkeratinized stratified squamous avascular epithelium, lending stability to the graft while the thin submucosa permits early revascularization. Additionally, the team has a history of success with the use of BMG in urethroplasty.

“To our knowledge, this is the first reported use of BMG in RnVF repair,” says Cecile Ferrando, MD, MPH, Director of Cleveland Clinic's Female Pelvic Medicine & Reconstructive Surgery Fellowship program and Director of Cleveland Clinic's Transgender Surgery & Medicine program.

“We were pleased when the patient reported good sensation in her neovagina, and no leakage of stool or gas from the vagina at her three-month follow-up appointment,” says Molly DeWitt-Foy, MD, a resident in the Glickman Urological & Kidney Institute's Department of Urology.

Fluoroscopic images of a radio-opaque enema showed that there was no connection between the neovagina and the rectum. Exam and proctoscopy in the operating room confirmed adequate repair of the fistula, and the patient's ileostomy was reversed.

Six months later, the patient reported good urinary, bowel and vaginal function with no symptoms of RnVF recurrence. At this point, the patient was permitted to begin vaginal dilation up to three times daily.

#### **Penile inversion neovaginoplasty**

Gender affirmation surgery, such as neovaginoplasty, may complement hormone therapy in order to reduce gender dysphoria and improve quality of



The fistula was confirmed with preoperative flexible sigmoidoscopy.

life for transgender women. The penile inversion neovaginoplasty technique involves use of the penile skin and a scrotal graft to create a functional neovaginal tube, which is inset in the vesicorectal space, a potential space that is created through a transperineal dissection. The external genitalia are created using penile skin, a portion of the urethral mucosa and the penile structures including the glans penis.

Postoperatively, the reconstructed anatomy is functional and sensate. Surgical risks include bleeding and need for transfusion; postoperative hematoma, seroma and infection; and intraoperative rectal, bladder and urethral injury, with risk for postoperative fistula formation between these organs and the neovagina.

“Following surgery, our patients are admitted to the hospital for three nights and remain on bed rest, allowing their flaps to heal properly,” Dr. Ferrando explains. “Most of our patients are from out of state, and require extended recovery time before returning home. Following discharge on postoperative day three, patients go to an on-campus hotel, where they are observed for four to 10 nights. We ensure that our patients are healing properly and get the wound care they need for favorable outcomes.”

## The Profound Impact of Philanthropy in Women's Health Research

### Announcing the Lilli and Seth Harris Endowed Chair for Ovarian Cancer

Ovarian cancer is a leading cause of cancer death in women, and research remains underfunded on a national level. With the help of a generous philanthropic gift, Cleveland Clinic's Ob/Gyn & Women's Health Institute (WHI) hopes to make a significant difference in women's lives by answering questions that may not be addressed otherwise.

The Lilli and Seth Harris Endowed Chair for Ovarian Cancer will provide ongoing financial support for current and future endeavors in ovarian cancer research, education and prevention programs at main campus and Cleveland Clinic Cancer Center at Hillcrest Hospital.

“This contribution will have a profound impact,” states Beri Ridgeway, MD, Chair of the WHI. “Philanthropy is important in all aspects of women's health, which is typically underfunded. We use philanthropic funds to promote our research, education and clinical care. It's hard for novel research projects and clinical programming to be successful without adequate funding. This generous gift will be transformative for our work in ovarian cancer.”

#### **Ovarian cancer research is desperately needed**

In the U.S., the rate of new cases of ovarian cancer is 11.2 per 100,000, with a death rate of 6.7 per 100,000. That's 21,000 new cases of ovarian cancer each year. With a five-year relative survival rate of 48.6%, the prognosis is generally poor for women who develop ovarian cancer. The disease accounts for nearly 14,000 deaths annually. The median age at diagnosis is 63 years old, and risk factors include older age, early menarche or late menopause, nulliparity, endometriosis, asbestos exposure and genetic predisposition.

“Ovarian cancer is one of the unfortunate diseases that we find late, mostly because the symptoms are

vague and appear later in the disease. Generally speaking, we diagnose ovarian cancer in stage 3 or 4 about 75% of the time,” says Chad Michener, MD, gynecologic oncologist and Medical Director for Continuous Improvement for the WHI.

Research is ongoing, and more is desperately needed related to identifying biomarkers, elucidating mechanisms of chemoresistance and developing targeted therapies.

#### **For WHI, the second endowed chair in gynecologic cancers**

This is the second endowed chair in gynecologic cancers in the WHI. The first, announced in 2019, was the Laura J. Fogarty Endowed Chair in Women's Health for Uterine Cancer Research. Robert DeBernardo, MD, Director of the Peritoneal Surface Malignancy Program, holds this position.

“An endowed chair like the Lilli and Seth Harris Endowed Chair for Ovarian Cancer will allow us to recruit a new clinician scientist to our department. With a great group of gynecologic oncologists, busy clinic locations and research funding, it's an attractive position,” says Dr. Ridgeway.

Once identified, the Lilli and Seth Harris Endowed Chair for Ovarian Cancer will work at both main campus and Hillcrest Hospital in order to provide continuity of cutting-edge care between the two sites. Other gynecologic oncologists — Robert DeBernardo, MD, Chad Michener, MD, and Stephanie Ricci, MD — also see patients at both sites.

If you are interested in discussing this position, please reach out to the Cleveland Clinic Office of Physician Recruitment (visit <https://my.clevelandclinic.org/professionals/provider-recruitment>).

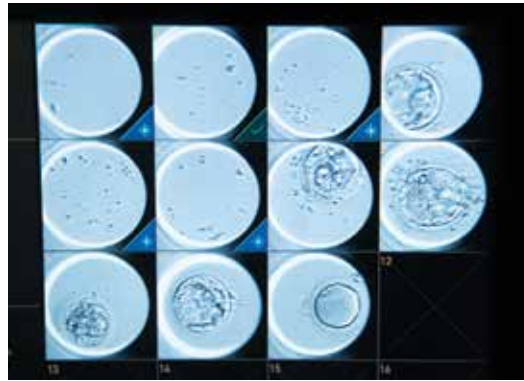
## Uninterrupted Culture in Time-Lapse Incubator Supports Human Embryonic Development

### Large randomized study compares embryo growth kinetics and live birth rates between culture media

In vitro fertilization (IVF) has been vastly improved over the past few years with a transition to blastocyst state cryopreservation and transfer, according to Nina Desai, PhD, HCLD, IVF Lab Director at Cleveland Clinic. “Our IVF program now does 100% blastocyst stage transfers, which requires confidence in the culture system as well as significant laboratory skill to create high-quality embryos capable of growing in vitro for five to six days.”

Dr. Desai also reports that the IVF lab at Cleveland Clinic now performs mostly single embryo transfers, which has reduced the rate of multiple pregnancies. Another trend is a shift toward performing more frozen rather than fresh embryo transfers. “Cryopreservation by vitrification has been a major factor in improving embryo survival and implantation potential,” she explains. “We use a special device called the Rapid-i™ Vitrification System that allows us to freeze an embryo by suspending it in  $< 1 \mu\text{L}$  of fluid, which permits extremely rapid cooling to  $-196^\circ\text{C}$ . In turn, these rapid cooling and warming rates prevent ice crystallization and damage to the embryo. With this new technique, our pregnancy rate with frozen embryos is now equal to, or sometimes higher than, that of fresh embryo transfers.”

A factor that favors use of frozen embryos over fresh is that it allows clinicians to prepare a more physiologically receptive uterine environment, since the embryo transfer is not done during the same cycle as the ovarian stimulation, explains Elliott G. Richards, MD, Director of Reproductive Endocrinology and Infertility Research in Cleveland Clinic's Ob/Gyn & Women's Health Institute.



### Comparative study of culture media

To further advance IVF practice, Drs. Desai and Richards, along with colleagues Meng Yao, MS, and Jeffrey M. Goldberg, MD, recently conducted the largest prospective randomized study to date of embryo development and live birth rates between sibling embryos cultured in two different single-step media.<sup>1</sup>

“We examined and compared the dynamics of embryo growth in more than 10,000 embryos,” Dr. Desai says. Sibling embryos were divided randomly between two different single-step culture media (G-TL™ and global media). Timing of embryonic genomic activation and ultimately progression to blastocyst were observed using a time-lapse (TL) incubator, which allows continuous, undisturbed culture without medium refreshment. The advantages of a TL incubator over a traditional incubator are that embryologists can constantly monitor the embryos hands free, observe any anomalous events and make more objective comparisons of embryos having similar morphologies at a specific time by viewing TL video footage. “We believe that using a single-step medium and the TL incubator may reduce stress on an embryo,” she reports.

The study persisted for two and a half years, proceeding to embryo implantation and analysis of live birth rates and birth weight.

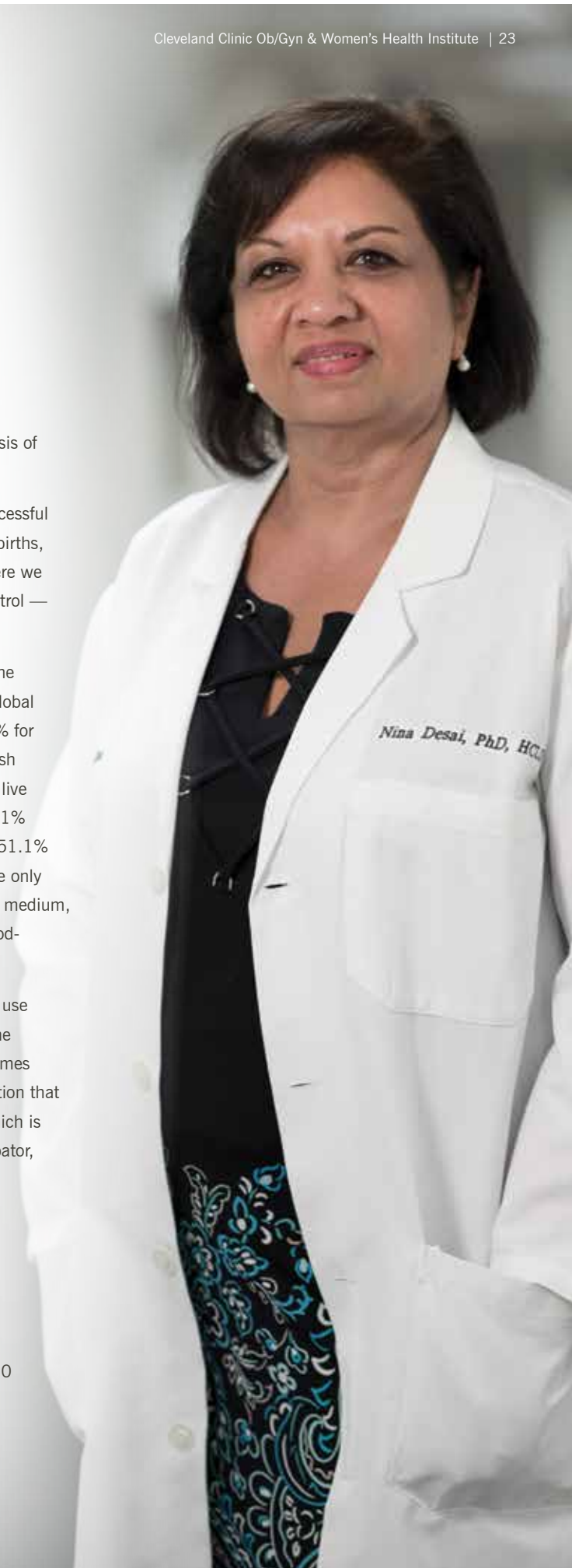
“There are many variables that go into the successful growth of embryos, pregnancy rates and live births, many of which are beyond our control, but here we examined an important variable we could control — the culture media,” says Dr. Richards.

The results showed little difference between the two culture media in terms of implantation (global medium, 58.7% for fresh embryos and 64.1% for frozen embryos; G-TL medium, 61.7% for fresh embryos and 60.5% for frozen embryos) and live birth rates (54.2% for fresh transfers and 53.1% for frozen transfers with global medium, and 51.1% and 50%, respectively, for G-TL medium). The only observed difference was that culture in global medium, resulted in an overall higher percentage of good-quality blastocysts for cryopreservation.

Dr. Richards notes that as more labs move to use of a TL incubator, having information about the optimal choice for a single-step medium becomes more important. “It's clinically useful information that the global medium and the GT-L medium, which is specially formulated for use with the TL incubator, are comparable in terms of the outcome that matters most — live birth.”

### Reference:

<sup>1</sup> Desai N, Yao M, Richards EG, Goldberg JM. Randomized study of G-TL and global media for blastocyst culture in the EmbryoScope: morphokinetics, pregnancy, and live births after single-embryo transfer. *Fertil Steril*. 2020 Dec;114(6):1207-1215.





## Prenatal Group Program Improves Pregnancy Outcomes

### 'Centering' approach lowers rate of preterm birth and increases breastfeeding

The most recent data from the Centers for Disease Control and Prevention indicate that approximately 10% of infants in the United States are born preterm annually<sup>1</sup> and approximately 83% of mothers start breastfeeding after delivery.<sup>2</sup> In 2019, outcomes for mothers in Cleveland Clinic's CenteringPregnancy program were much better: a 4% rate of preterm birth and 92% breastfeeding at discharge.

Those numbers tell the story of the significant impact that "centering" — a unique form of supportive prenatal care that involves group appointments — can have on both mothers and their babies.

"Centering involves a totally different level of patient education and connections with nurse-midwives and facilitators," says program manager Rasheeda Larkin, MPA. "For expectant mothers, the other women in the group are like pregnancy BFFs."

Centering has a demonstrated track record of providing improved outcomes among those choosing to participate. It also reduces healthcare costs, and patients report higher levels of satisfaction, according to Edward Chien, MD, MBA, Chair of the Department of Obstetrics and Gynecology and a maternal-fetal medicine specialist with Cleveland Clinic.

"These factors are some of the reasons we are looking to grow and expand our programs. Our community partners have been enthusiastic about our continued expansion into the community," Dr. Chien says.

#### Reducing stress and building support systems

During the CenteringPregnancy program, the expectant mothers learn about many aspects of pregnancy, delivery and infant care from specially trained nurse-midwives and from each other. Guest speakers provide information on lactation and how to care for newborns. Each woman also receives a private check-in with her midwife at each session.

There is also a special focus on normalizing breastfeeding, because of what Ms. Larkin describes as the approximately 30% lower rate of initiating breastfeeding among Black women than among white women. "In the Black community, there is a lack of education about breastfeeding and a stigma around it," she says. "The group allows us more time to talk to women and normalize the practice so they can be successful with breastfeeding."

By the end of 2020, CenteringPregnancy program groups will be available in six locations: Cleveland Clinic's Akron General, Lakewood Family Health Center, Lorain Family Health & Surgery Center, South Pointe Hospital, Stephanie Tubbs Jones Health Center and Westlake Family Health Center. The expansion from the initial pilot was made possible, in part, by a grant from the March of Dimes as part of Cleveland Clinic's efforts to reduce infant mortality in the community.

Plans are in the works to continue to expand the number of CenteringPregnancy groups offered and outreach to additional underserved populations, such as women who are Latinas or immigrants.

#### References:

<sup>1</sup> Martin JA, Hamilton BE, Osterman MJK, Driscoll AK, Division of Vital Statistics. Births: final data for 2018. National vital statistics reports. 2019 Nov;68(13). Retrieved from [https://www.cdc.gov/nchs/data/nvsr/nvsr68/nvsr68\\_13-508.pdf](https://www.cdc.gov/nchs/data/nvsr/nvsr68/nvsr68_13-508.pdf). Accessed September 29, 2020.

<sup>2</sup> Centers for Disease Control and Prevention. Key statistics from the national survey of family growth – B listing. National survey of family growth. Retrieved from [https://www.cdc.gov/nchs/nsfg/key\\_statistics/b\\_2015-2017.htm#initiation](https://www.cdc.gov/nchs/nsfg/key_statistics/b_2015-2017.htm#initiation). Accessed September 29, 2020.

## Complicated Pregnancies Benefit From a Team Approach

### What's next for maternal-fetal medicine?

The subspecialty of maternal-fetal medicine evolved from the need to provide special care for the growing number of women with medical complications of pregnancy, including those with fetal abnormalities. One consequence is that women born with congenital heart defects are now surviving into adulthood and wish to become pregnant.

"Many still have issues that complicate their pregnancy or increase the risk of morbidity and mortality," says Edward Chien, MD, MBA, who was appointed Chair of the Department of Obstetrics and Gynecology in December 2019.

Maternal-fetal medicine specialists also provide care for pregnant women at increased risk due to medical conditions such as cystic fibrosis, cancer, hypertension, diabetes, Crohn's disease, autoimmune diseases and seizure disorders, as well as those who are older or have a history of pregnancy complications.

More recently, Cleveland Clinic maternal-fetal medicine specialists have assumed a unique role in helping women who have undergone uterine transplantation go through pregnancy and delivery.

### Improving birth outcomes

The widespread use of ultrasound for prenatal screenings enables many fetal abnormalities to be diagnosed in utero. At Cleveland Clinic, maternal-fetal medicine specialists partner with obstetricians to care for babies with abnormalities that may involve the heart, digestive system or central nervous system.

Today, a number of fetal interventions are possible that can improve birth outcomes. "Specialists in our Fetal Surgery Program repair myelomeningocele and other significant issues. We then follow the mother through pregnancy and delivery," says Dr. Chien.

A new addition to this program is a fetal laser specialist who treats twin-to-twin transfusion syndrome. This condition, in which twins share a blood supply across the placenta, carries a high mortality risk for one or both babies.

"The outcome is improved when the vessels are occluded to prevent the exchange of blood between the babies," says Dr. Chien.

### Special Delivery Unit

Cleveland Clinic obstetricians are available in 14 locations throughout Northeast Ohio. When it comes time to deliver, however, high-risk patients may be transferred to the Special Delivery Unit on main campus, where they can be closely monitored by maternal-fetal medicine specialists. The unit is located adjacent to the cardiac catheterization lab and cardiac intensive care unit and is convenient to all pediatric and adult subspecialists.

### What's next?

In their dedication to improving the health of pregnant women and delivering healthy babies, the Department of Obstetrics & Gynecology has undertaken several research initiatives.

They are piloting the use of telehealth to monitor patients with hypertension during pregnancy and postpartum. In addition, they are collaborating on a quality improvement project related to the management of patients with severe hypertension. Finally, they are partnering with colleagues at local hospitals on a study of COVID-19 and pregnancy. "We are hoping to identify the factors that might predict the risk of COVID-19 transmission to the fetus and their impact on maternal pregnancy outcomes," Dr. Chien says.

## Rigor and Opportunity in Tracking Residency Program

### Postgraduate training is a top priority for the Ob/Gyn & Women's Health Institute

In addition to receiving core training in the fundamentals of obstetrics and gynecology, residents at Cleveland Clinic tailor seven blocks of curriculum during the four-year program to meet their individual needs. "Our program allows people to choose what they would like to focus on in their careers, find ways to get individualized experiences and graduate with a special skill set," says Vicki Reed, MD, Vice Chair for Education in the Department of Obstetrics & Gynecology and Program Director of the residency.

The residency program, which is the only tracking Ob/Gyn program in the country, and the institute's six fellowship programs, help make Cleveland Clinic a sought-after destination for postgraduate education and training.

### Residency program is one of a kind

"The overarching goal of all our training programs is to put forth into the medical community physicians who are really well trained for both specialty (general) or subspecialty practice," says Dr. Reed. "We have a high surgical volume, compassionate clinicians and a strong research program — all of which foster the development of skilled surgeons and compassionate clinicians."

Last year, Cleveland Clinic received approximately 700 applications for seven residency spots in its Ob/Gyn program, which was launched in 2012. The tracking program allows residents to gain significant exposure to and a deeper understanding of numerous specialties and subspecialties.

(continued)





Residents run through a laparoscopic procedure with Clinical Assistant Professor Erin Higgins, MD, in Cleveland Clinic's Simulation Lab.

(continued)

“Our residents get to operate with nationally recognized subspecialty surgeons and more than 100 physicians in the region doing specialty or general cases,” says Dr. Reed. “That’s a huge opportunity for them to get diverse experience. They also have their continuity clinic at Westown, providing care in the community and gaining outpatient experience.” When residents complete the program, they move into competitive fellowship programs, specialty practice and academic specialty medicine.

The residency program is well regarded by physicians nationwide. In a survey of more than 72,500 physicians conducted by Doximity, an online networking service for medical professionals, Cleveland Clinic’s Ob/Gyn Residency Program ranked No. 11 in the country, No. 3 in the Midwest and No. 1 in Ohio.

#### **New fellowships added to postgraduate offerings**

The WHI currently offers six fellowship programs:

- Female Pelvic Medicine and Reconstructive Surgery
- Gynecologic Oncology
- Reproductive Endocrinology and Infertility
- Minimally Invasive Gynecologic Surgery
- Specialized Women’s Health
- Transgender Medicine and Surgery

In addition to the six fellowships, Cleveland Clinic completed a site review and is awaiting approval for a maternal-fetal medicine (MFM) fellowship. The three-year fellowship would include research work, as well as training in core MFM/ultrasound, labor and delivery, genetics, surgical intensive care, obstetric anesthesia and fetal surgery.

“The addition of the fellowship, as well as the growth of our division, will enhance our maternal-fetal medicine division,” says Uma Perni, MD, a physician in the Department of Obstetrics and Gynecology and Associate Program Director of the MFM Fellowship. “It is very important, particularly for northeast Ohio, to have well-trained MFM physicians due to high rates of maternal mortality and morbidity, preterm birth, health disparities, and infant mortality in our region.” Cleveland Clinic delivers more than 10,000 babies per year at two regional hospitals and a small Special Delivery Unit at main campus.

No matter the educational program, postgraduate training through the WHI is successful in large part due to two intangible factors: commitment and camaraderie. “We have a really strong dedication to education. People are willing to teach and to mentor residents and fellows,” says Dr. Reed. “And there is a lot of camaraderie. We really are a community that keeps wellness at the forefront.”

## Rethinking the Delivery of Ob/Gyn Care

What to expect from distance health going forward

By Amy Merlino, MD

**The COVID-19 pandemic radically changed healthcare delivery over a short period of time, and Cleveland Clinic's Ob/Gyn & Women's Health Institute (WHI) was well prepared for the challenges brought about by the ensuing rapid scaling of digital health.**

As an institute, we saw incredible growth in the percentage of virtual vs. traditional, in-person consults. Compared with the same time period in 2019, WHI's virtual visits were up 960% through August 2020. Even before the pandemic, Cleveland Clinic leadership activated a transition plan toward predominately remote care. In WHI, we had successful pilot models to follow.

Prior to the pandemic, we were aware of the increasing role of technology in healthcare. Despite early adoption of digital care by Cleveland Clinic, telehealth represented less than 2% of the total care — an experience not unlike that of other large healthcare organizations. Throughout the Cleveland Clinic enterprise, we were looking for more ways to fold virtual care into our practice.

Among WHI's first virtual offerings were prenatal visits. Led by Julian Peskin, MD, MBA, a group of providers began conducting virtual prenatal visits for low-risk obstetric patients a few years ago. Qualifying patients receive a Doppler ultrasound device and blood pressure cuff during their second trimester. These patients are instructed to measure their weight and blood pressure and listen to the fetal heart beat before each appointment.

The patients love the convenience of these visits — indicating that virtual visits reduced unnecessary stress related to any commute to the clinic, time away from work, childcare needs and exposure to viruses. It didn't take Dr. Peskin long to realize that some high-risk patients might benefit from the reduced stress and exposure of home monitoring as well.

### Rapid adoption and scaling

Toward the end of 2019, we were really challenging ourselves to think about how we could incorporate virtual visits into other aspects of our practice. And then came COVID-19.

As the pandemic evolved, it became apparent that Ob/Gyn providers would need to apply similar models of virtual care for patients, including infertility consults, preconception counseling, birth control discussions, preoperative counseling and surgical follow-up.

As an enterprise, our providers were quickly credentialed and trained to provide virtual care. We developed a Digital Health Playbook with tips and tricks for the entire care team — from schedulers to physicians — to ensure that our patients would continue to have access to appropriate and high-quality healthcare amid the pandemic. To further increase access for all patients during this unprecedented time, we made this playbook available to the public.

Since April, we rolled out a secure video service that is integrated into the digital health record. We were able to move virtual visits from the additional digital tools permitted for use during the health emergency and onto HIPAA-compliant platforms for individual virtual visits and shared medical appointments.

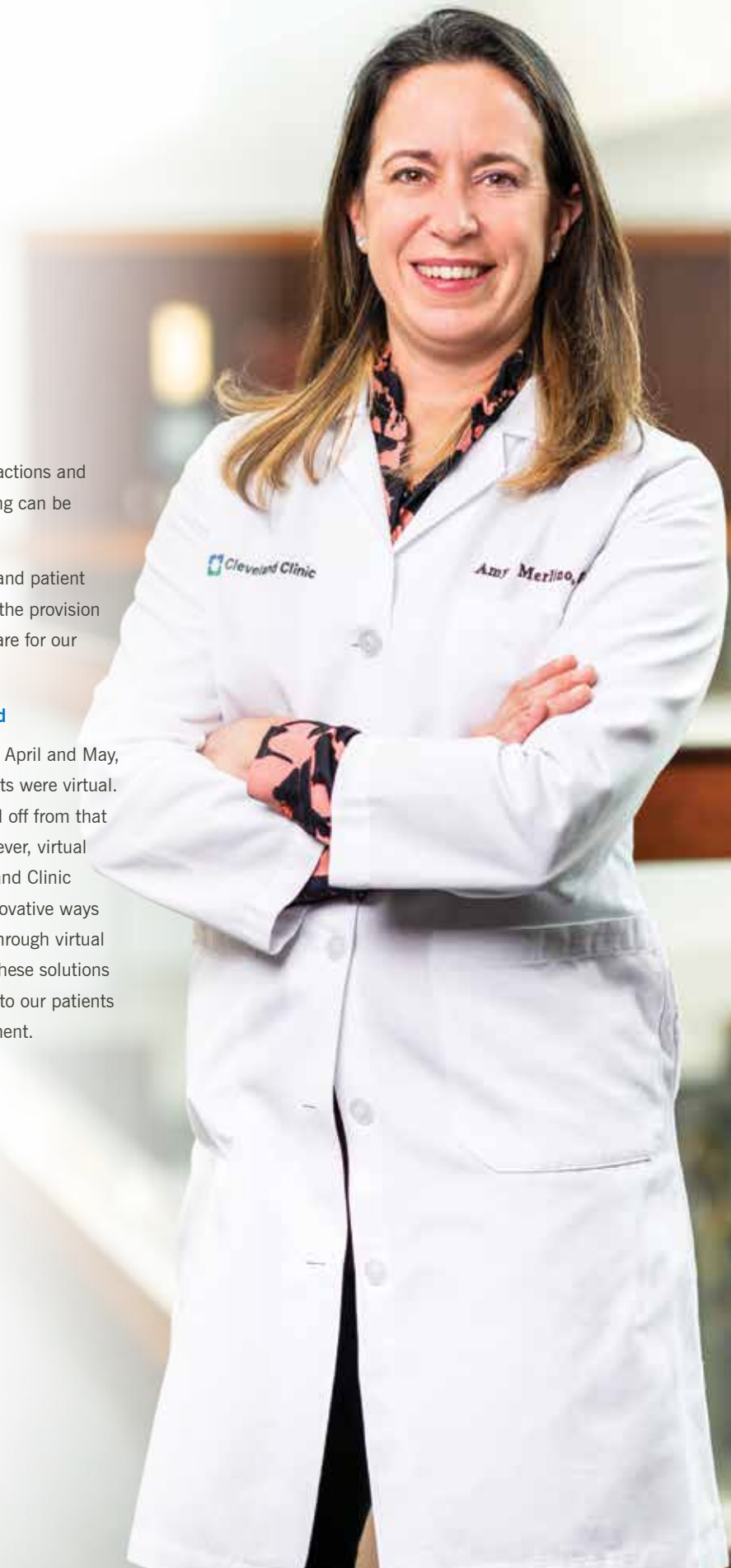
Additionally, we have also optimized the check-in process for virtual visits to allow for more functionality. We leveraged this eCheck-in when we brought patients back to the clinic for face-to-face

appointments to reduce interactions and ensure that physical distancing can be maintained.

We continue to track quality and patient experience metrics to ensure the provision of high-quality, appropriate care for our patients with virtual visits.

### What to expect going forward

At our peak of virtual visits in April and May, 60-70% of WHI's patient visits were virtual. Virtual volumes have dropped off from that point as we reactivated; however, virtual visits are here to stay. Cleveland Clinic continues to explore new, innovative ways to meet our patients' needs through virtual capabilities, and we believe these solutions will continue to deliver value to our patients in a post-COVID-19 environment.





## Ob/Gyn & Women's Health Institute At a Glance

### 13 centers across the region and in Florida

Chronic Pelvic Pain  
Endometriosis  
Fertility  
General Gynecology  
Gynecologic Infectious Diseases  
Gynecologic Oncology  
Maternal-Fetal Medicine  
Menstrual Disorders, Fibroids and  
Hysteroscopic Services  
Obstetrics and Family Maternity  
Postpartum Care Clinic  
Specialized Women's Health  
Urogynecology and Pelvic Floor Disorders  
Women's Weight Management

### Shared medical appointments

The Ob/Gyn & Women's Health Institute offers shared medical appointments in these centers:

General Gynecology | Obstetrics and Family Medicine  
| General Obstetrics and Gynecology, Florida |  
Menstrual Disorders, Fibroids and Hysteroscopic  
Services | Specialized Women's Health |  
Urogynecology and Pelvic Floor Disorders | Women's  
Weight Management

### Virtual visits

Virtual visits allow patients to communicate in real time (audio and video) with their providers from their home, office or elsewhere via a computer or smartphone. The Ob/Gyn & Women's Health Institute offers virtual visits for its Metabolic Weight Management Program and for new, follow-up and postoperative visits in a variety of services.

### Clinical research: by the numbers

\$3.8 million in new research funding  
205 studies  
96 publications

### Patient activity

Hospital admissions	10,912
Surgical procedures performed*	8,140*
Deliveries	9,694
Outpatient visits	387,837
Shared medical appointments	872
Virtual visits	27,031

### Caregivers

Ob/Gyns	157
Certified nurse midwives	28
Advanced practice nurses	43
Residents	25
Fellows	13

\*Excludes cesarean sections

Statistics reported are from July 1, 2019, to June 30, 2020.



## Resources for Physicians

### Join us for Controversies in Endometriosis, Adenomyosis and Fibroids

A series of 15 on-demand webcasts, beginning with a CME-certified live stream course on Friday, March 19 and Saturday, March 20, 2021. Visit [ccfcme.org/endometriosis21](http://ccfcme.org/endometriosis21) to register.

### Consult QD — Ob/Gyn & Women's Health

News, research and perspectives from Cleveland Clinic experts:  
[consultqd.clevelandclinic.org/obgyn](http://consultqd.clevelandclinic.org/obgyn)

### Ob/Gyn ePerspectives

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### CME Opportunities

Visit [ccfcme.org](http://ccfcme.org) for offerings from Cleveland Clinic's Center for Continuing Education.

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The Ob/Gyn & Women's Health Institute provides a full spectrum of care for women from adolescence through mature adulthood. Caregivers provide collaborative care for gynecological cancers, infertility, incontinence, pelvic floor disorders and other women's health issues in a supportive environment enhanced by innovative research. The institute is part of Cleveland Clinic, a nonprofit, multispecialty academic medical center integrating outpatient and hospital care with research and education for better patient outcomes and experience. More than 4,500 staff physicians and researchers provide services through 20 patient-centered institutes. Cleveland Clinic is currently ranked as one of the nation's top hospitals by *U.S. News & World Report*. [clevelandclinic.org](http://clevelandclinic.org)

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