The uterus is one of the body’s most plastic organs. During a full-term pregnancy, its volume increases over 1000-fold as it grows from the size of a fist to the size of a watermelon. Then, once pregnancy ends, the process reverses as the uterus shrinks back to its original size.

To accommodate this plasticity, myometrial cells must undergo significant hyperplasia and then return to a quiescent state. It is possible that this extreme plasticity makes the uterus vulnerable, leading to one of gynecology’s most common and challenging conditions: uterine fibroids. These noncancerous uterine tumors affect the majority of women over their lifetime—up to 70 percent of whites and 80 percent of blacks by age 50—causing, for some, extreme pain, fertility issues and bleeding severe enough to require blood transfusions.

Despite the pervasive and serious nature of this problem, few good treatments for fibroids exist, says James Segars, director of the Division of Reproductive Sciences and Women’s Health Research in Johns Hopkins’ Department of Gynecology and Obstetrics. For example, even though hysterectomy offers a permanent solution, it’s major surgery that isn’t an option for women who aren’t finished having children. Fibroid embolization, on the other hand, is less invasive, but this treatment leaves the possibility of fibroid regrowth and a return of symptoms.

That’s why Segars and his colleagues are working on new treatments that attack this problem in a completely different way, based on their long-term research into why fibroids form.

Although no one knows exactly why fibroids arise and grow, Segars and his team have gradually gathered clues through a decade of laboratory research. One of their key studies showed that a bevy of genes are dysregulated in cells that compose fibroids, but those most affected appear to be responsible for excreting the extracellular matrix. Other affected genes include those involved in mechanical signaling.

Functions of these two sets of genes are intimately intertwined in creating fibroids, Segars explains. When there’s an excess of extracellular matrix, the cells become under mechanical stress. Because their intrinsic mechanical signaling is abnormal, they multiply, leading to even more accumulation of extracellular matrix.

“It’s like they’re in an open feedback loop similar to the hyperplasia of pregnancy,” Segars says. “Attacking aspects of this process could lead to new treatments for fibroids, he adds. He and his team are working on a novel enzymatic treatment that could be injected into fibroids, dissolving the abnormal extracellular matrix and, thus, causing the fibroids to shrink or disappear.

“Many women don’t realize that the extreme pain and bleeding that they’ve had since the start of their periods isn’t normal,” Segars says. “We want to offer them a better option to discover how great normal can be.”

For more information or to refer a patient: 443-997-0400
To Prevent Pelvic Organ Prolapse

Affecting millions of women in the U.S., pelvic organ prolapse is often chronic, beginning during the childbearing years and lasting for decades with urinary and fecal incontinence, and other unpleasant symptoms. Despite a bevy of treatment options, none are consistently effective at relieving symptoms for all women.

Each of these factors makes prolapse the “poster child” for the need for prevention, says Victoria Handa, who directs both the Department of Gynecology and Obstetrics at Johns Hopkins Bayview Medical Center and the Female Pelvic Medicine and Reconstructive Surgery Division.

However, she adds, there’s one glaring hitch: No one knows what causes pelvic organ prolapse in the first place, so no one knows how to stop it before it happens.

That’s why Handa and her colleagues have led an ongoing, National Institutes of Health-funded study since 2008 looking at what factors influence the risk of prolapse. The study has followed 1,500 women, each of whom has delivered at least one child. Participants represent all childbirth scenarios: planned cesarean, cesarean after labor began, cesarean in the second stage of labor, vaginal delivery without assisted extraction, vaginal delivery with forceps or a vacuum cup. Through physical exams and questionnaires to assess symptoms of pelvic floor disorders, Handa and her colleagues discovered that the primary factor that affects the risk of prolapse is a single vaginal delivery—with chances dramatically increased with the use of forceps or vacuum.

Wondering how vaginal delivery affects the pelvic muscles, Handa and her team also used a perineometer to assess volunteers’ pelvic muscle squeeze strength. For those who had had at least one vaginal delivery, squeeze strength was about 30 percent less than those who had never had a vaginal delivery. Those whose vaginal delivery involved forceps or a vacuum cup had squeezes 30 percent weaker still.

“This makes us think that pelvic muscles are an important key,” Handa says.

Most recently, the team invited volunteers to undergo 3D transperineal ultrasounds. Thus far, they’ve collected hundreds of videos that allow them to examine how the pelvic muscles look and behave when the volunteers contract them, bear down or perform other activities. Combined with other data the researchers have collected, these movies provide a wealth of anatomical information from every angle.

Eventually, Handa says, their work may lead to new treatments for prolapse—or, ideally, a way to prevent it altogether. “There are 4 million deliveries in the U.S. each year,” says Handa. “We see each of them as an opportunity to help women avoid this problem.”

For more information or to refer a patient: call 410-550-4406

Life-Saving Simulations

Even when complications arise, few pregnancies and deliveries are life-threatening. But in very unusual instances, conditions such as amniotic fluid embolism, thyroid storm or myocardial infarction in pregnancy can quickly endanger both mother and child. Although these situations are still rare, their incidence is growing as women delay childbearing late into their reproductive years, increasing the risk of comorbidities.

“In obstetrics, 99 percent of the time we don’t expect to take care of something that becomes a critical care case acutely,” says Andrew Satin, director of the Johns Hopkins Department of Gynecology and Obstetrics. “You can’t train for these things while they’re happening. You just have to know how to do it.”

That’s why Satin and Hopkins colleagues from specialties including obstetrics and gynecology, maternal-fetal medicine, neonatal intensive care, anesthesiology, nursing and others have created video simulation trainings on more than a dozen rare but critical conditions that can arise during pregnancy and delivery.

To develop the videos, partially funded by a grant from the Society for Maternal-Fetal Medicine, Satin and his colleagues worked with experts from Johns Hopkins and elsewhere to decide key teaching points and write scripts for each simulation. All videos were taped at Johns Hopkins’ state-of-the-art simulation center, with help on production values from Hopkins maternal-fetal medicine fellow Clark Johnson, who was a drama major as an undergraduate.

The fact that the Society for Maternal-Fetal Medicine chose Hopkins to create the videos is a reflection of its long history as a tertiary care center for these rare conditions as well as a leader in simulation training. “We do simulation training for all levels of education, from undergraduate medical education to graduate, postgraduate and continuing education,” Satin says.

Several years ago, he and his colleagues also developed simulation training for managing shoulder dystocia, a program now used by many hospitals across the country.

“These simulations,” says Satin, “are valuable tools in our efforts to reduce patient harm and ensure quality and safety.”
When Cancer and Pregnancy Intersect

Options for Kulp included allowing the pregnancy to proceed without intervention, delivering a course of chemotherapy during pregnancy, or delivering the baby through cesarean section to avoid the fungating mass and performing a concurrent radical hysterectomy. The last option provided the most positive prognosis for Kulp but would increase risk to the baby.

Fader worked with maternal-fetal medicine colleague Linda Szymanski, medical director of labor and delivery and inpatient obstetric services at The Johns Hopkins Hospital, as well as others in neonatology and anesthesiology to ensure that Kulp received extensive counseling to help her make the most informed decision.

Kulp elected early delivery and radical hysterectomy. After she received steroids to speed fetal lung maturity, her baby boy, Kayden, was delivered without complication at 30 weeks’ gestation, and Fader performed a radical hysterectomy and surgical debulking procedure that included staging biopsy of the lymph nodes and removal of large tumor masses in the ovary and bowel mesentery.

Although each member of the care team agreed that early delivery wasn’t ideal, Kayden had an uncomplicated hospital stay, leaving after just four weeks. After surgery, Kulp received an innovative course of chemotherapy during pregnancy, or delivering the baby through cesarean section to avoid the fungating mass and performing a concurrent radical hysterectomy. The last option provided the most positive prognosis for Kulp but would increase risk to the baby.

“Having the privilege of collaborating with an exceptional treatment team to help women like Ashley Kulp live the best, most meaningful life possible—it doesn’t get any better than that,” says Fader.

Ashley Kulp today with her healthy, active 2-year-old, Kayden.

Center for Rare Gynecological Cancer

“WE’VE LEARNED THAT INDIVIDUALIZING THE APPROACH TO EACH PATIENT IS CRITICAL.” —AMANDA NICKLES FADER

Delivery on ECMO

With conventional techniques to improve Chung’s lung failure and airway bleeding unsuccessful, her care team decided to place her on extracorporeal membrane oxygenation. Using ECMO during pregnancy isn’t unprecedented; Vaught notes a few cases in the literature describing its use for pregnant patients who had influenza and other acute respiratory issues. “There’s good data,” he says, “that pregnancy is not a contraindication.”

However, Vaught adds, there’s little information about delivery on ECMO. But as Chung’s condition continued to worsen, it looked increasingly like that would be her only option, even though her fetus was now only about 24 weeks’ gestation. Escalating blood pressures along with proteinuria suggested that Chung was becoming preeclamptic.

“No one wants to deliver a baby who’s that preterm,” Vaught says. “But we knew that’s what needed to be done.”

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Welcome

Jeanne S. Sheffield, M.D.
Director of the Division of Maternal-Fetal Medicine

Formerly at the University of Texas Southwestern Medical Center, Jeanne Sheffield is an internationally recognized expert in sexually transmitted disease in pregnancy, a member of the American Board of Obstetrics and Gynecology Division of Maternal-Fetal Medicine and a member of the board of directors of the Society of Maternal-Fetal Medicine. She is also an editor of Williams’ Obstetrics, a reviewer for numerous organizations and journals, and an adviser to the Centers for Disease Control and Prevention and the National Institute of Child Health and Human Development.

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JOHNS HOPKINS Gynecology

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JOHNS HOPKINS Gynecology

NEWS FROM THE JOHNS HOPKINS DEPARTMENT OF GYNECOLOGY AND OBSTetrics

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