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The YOGS Journal is published yearly by the Yale School of Medicine, Department of Obstetrics, Gynecology and Reproductive Sciences, PO Box 208063, FMB 337, New Haven, Connecticut 06520-8063.

Tel: 203-737-4593; Fax: 203-737-1883

http://medicine.yale.edu/obgyn/yogs/index.aspx

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Cover Photo: Sheffield-Sterling-Strathcona Hall
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EDITOR’S NOTE

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As upbeat as I always am, I fear the most notable event in our Department this year was a loss – the passing of Dr. Joel Silidker. Joel, who passed away in July, could have been described as the soul of our Department, ever since he arrived at Yale-New Haven Hospital in the fall of 1978 as a sub intern on the high-risk obstetrical service. Sue Richman’s eloquent note (see “In Fond Memory” on page 57) really describes, as best one can in writing, Joel’s vibrant persona. So it is to his memory that I would like to dedicate this volume.

We have otherwise had another excellent year in New Haven. Our YOGS event last year, celebrating the career of Dr. Roberto Romero, brought many of the most notable obstetrically related practitioners in the country back to New Haven, proving once again that there is really only one degree of separation between any important Ob/Gyn and Yale.

Dr. Hugh Taylor has fully assumed the leadership of our Department. We continue to attract terrific new house staff. (In only two days of interviewing candidates this year, I could have fully staffed our internship year from the 12 kids I interviewed.) We are also going to be expanding the residency to eight house officers a year because of the full integration of the Hospital of Saint Raphael into the Chapel Street Campus.

We are close to finalizing our section heads in perinatology and urogynecology. In the meantime, we have forged a closer bond with the Department of Urology, which has some new folks very interested in women’s health.

We continue to bring in very exciting experts in Ob/Gyn and related fields to educate us at grand rounds, and for those of you not able to attend, we are including highlights of their talks.

Of course I am delighted to welcome Dr. Leon Speroff back to Yale as our 2014 YOGS honoree, celebrating the 40th anniversary of the release of the Yale “Bible.” Dr. Nathan Kase will also join us for the event.

And speaking of anniversaries, as we prepare for the 50th anniversary of Griswold v. Connecticut, one of our rising young house officers, Dr. Abigail Cutler, has written a brief history of Family Planning at Yale, including interviews with our Family Planning attendings.

So thanks for spending some time with your Department, and we all hope that you will visit with us in person.

Mary Jane Minkin, MD, FACOG
HISTORICAL NOTE

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Family Planning at Yale: Past and Future

On November 10, 1961, Dr. C. Lee Buxton – Chair of the Department of Obstetrics and Gynecology at Yale – was arrested and fined $100. His crime? Providing contraception to married couples.

The story of a woman’s right to birth control in this country is a long and sometimes sordid one – and much of it took place in our very own backyard. For a married woman living in Connecticut in 1961, having access to contraception required money, a willing provider and enough gumption to break the law. For an unmarried woman, the options were dismal at best. Estelle Griswold, once described as the “stiff-spined” executive director of the Planned Parenthood League of Connecticut, had spent years challenging Connecticut’s archaic state law that prohibited the use of “any drug, medicinal article or instrument” to prevent pregnancy.

By 1961, Connecticut was the only state in the union to prohibit its citizens from using birth control – a distinction it had held for more than 25 years. In Dr. Charles Lee Buxton, Griswold found a sympathetic physician and a partner for her efforts to give women control over their reproductive lives.

To test the validity of the state law, Griswold and Buxton opened a clinic at the corner of Whitney and Trumbull streets in what amounted to nothing less than a dare. Nine days later the police showed up and made their arrests, setting in motion a case that would eventually make its way to the United States Supreme Court as _Griswold v. Connecticut_. In 1965, the Court declared the Connecticut law unconstitutional on the basis of privacy and thus paved the way for a number of subsequent landmark decisions concerning reproductive health, including _Eisenstadt v. Baird_ – which extended the right to obtain birth control to unmarried women – and _Roe v. Wade._

(For a wonderful perspective on _Griswold v. Connecticut_, look no further than to former Yale resident Gary Gross, who in 2011 wrote about the topic in these very pages: [http://medicine.yale.edu/obgyn/yogs/87_179528_Gross_Griswold_CT.pdf](http://medicine.yale.edu/obgyn/yogs/87_179528_Gross_Griswold_CT.pdf).)

Indeed, the Nutmeg State has come a long way since 1961. And, in fact, when it comes to providing access to reproductive health, Connecticut is now widely considered to be a
leader. Our small state houses no fewer than 17 Planned Parenthood health centers, and it earns an A grade from the NARAL Pro-Choice America for its legislation on reproductive health. But as anyone with access to a newspaper knows, the legacy of Roe v. Wade is under constant threat: Since 2011, states have enacted more than 205 restrictions on abortion – one of the most common surgical procedures for American women. To make matters worse, the number of abortion facilities in the U.S. now hovers around pre-Roe numbers, and in 87% of U.S. counties (home to 33% of American women) there is no abortion provider.

Many departments of obstetrics and gynecology across the country have been working to change that, spearheading an effort whose movement – as described by one writer for The New York Times – is “to integrate abortion [into residency training] so that it’s a seamless part of health care for women – embraced rather than shunned.” Part of this integration is mandated; since 1995, the Accreditation Council for Graduate Medical Education has required abortion training for all Ob/Gyn residency programs seeking ACGME accreditation. An even more important moment came four years later by way of the Ryan Program, a national initiative founded at the University of California at San Francisco in 1999 that provides resources and technical expertise to departments of obstetrics and gynecology to establish a formal rotation in Family Planning during residency. At medical centers with Ryan Programs, medical students and Ob/Gyn residents not only gain experience in performing both medical and surgical abortions; they learn how to manage terminations for women with pregnancies complicated by medical conditions and fetal anomalies, how to provide effective and compassionate pre- and post-procedure counseling and follow-up, and how to offer evidence-based contraceptive counseling and services, especially for women with complex medical problems.

To foster and promote the field of Family Planning in academic medicine, the Fellowship in Family Planning was developed. This program is a two-year fellowship, which offers subspecialist training in research, teaching and clinical practice in abortion, contraception and miscarriage care as well as public policy and advocacy training. Fellows are expected to graduate with a master’s degree in public health or science, complete research, gain experience in teaching and participate in global family planning activities abroad. The fellowship’s focus on high-quality research has also been recognized by numerous Obstetrics & Gynecology Pitkin Awards: In 2013, two of the three prizes were given to faculty associated with the fellowship. There are currently 28 Family Planning fellowship sites in academic institutions around the country, including Harvard, Columbia, Stanford and Johns Hopkins.

In 2005, Yale became a Ryan Program grantee and is now one of 65 U.S. medical centers that offer a dedicated rotation in Family Planning for their residents. In 2011, the Department hired two new physicians, Dr. Nancy Stanwood and Dr. Aileen Gariepy, to launch a Section of Family Planning. Among their top priorities is to secure a Family Planning fellowship at Yale. (The application was submitted in December 2013 and is currently pending.) Both attendings have become fast favorites among the residents for their mentorship and teaching.

“Dr. Gariepy and Dr. Stanwood are huge assets to the Department and to resident education,” said Jonathan Black, PGY-4. “They are excellent educators and excellent surgeons who provide residents with exceptional training – from contraception counseling for medically complicated patients to how to medically and surgically care for patients requesting termination of pregnancy at advanced gestations.”

“They took time out of their busy schedules to coach me through the creation and implementation of a hospital protocol for medical management of early pregnancy failure as well as the development of a community-based clinical research project on emergency contraception,” added Lissa Yu, PGY-2. “They are teaching the true art of being a physician-scientist: not just
what the questions should be, but how to ask them and how to approach finding the answers. In short, they are the very type of doctors I hope to become.”

Dr. Nancy Stanwood, Associate Professor and Section Chief of Family Planning, completed her training at the University of Michigan and through the Robert Wood Johnson Clinical Scholars Program Fellowship at the University of North Carolina. Most recently, she spent 10 years building and directing the Family Planning service at the University of Rochester. Dr. Aileen Gariepy, Assistant Professor in the sections of Family Planning and Comparative Effectiveness Research and a Yale Center for Clinical Investigation Scholar, hails from Pennsylvania, having completed her residency at Thomas Jefferson and a Family Planning fellowship at Magee Women’s Hospital. Recent research coming out of the section includes examining the comparative effectiveness of hysteroscopic vs. laparoscopic sterilizations, the cost-effectiveness of immediate postpartum vs. delayed contraceptive implant insertion, and the relationship between pregnancy intention and preterm birth.

“Yale’s Department of Obstetrics and Gynecology has made numerous historically significant contributions to the field of Family Planning,” noted Chairman Hugh Taylor. “Among those faculty members who made the greatest impact were Drs. John McLean Morris and Gertrude Van Wagenen, who were the first to use post-coital contraceptives in monkeys and then women. Today, Yale continues to shape the field in both research and patient advocacy. The addition of Drs. Nancy Stanwood and Aileen Gariepy to the Family Planning section has reinvigorated the section’s commitment to women’s reproductive freedom. New research and training programs will continue to keep Yale at the forefront of this critical field.”

Interview with Drs. Nancy Stanwood and Aileen Gariepy

I had a chance to chat with Drs. Gariepy and Stanwood about their first two years in New Haven, the future of family planning at Yale and their plans to commemorate the 50th anniversary of Griswold v. Connecticut.

Tell me about your decision to pursue a career in Family Planning. What or who has inspired you along the way?

AG: “If you have come to help me, you can go home again. But if you see my struggle as part of your own survival, then perhaps we can work together.” I used that quote as the beginning of my essay for medical school applications. I wanted to go to medical school to become an obstetrician/gynecologist because I wanted to support women. It was and continues to be my calling. I know that women are amazing and strong and resilient. And I believe that through twists of fate and flips of coins, we are all just a step away from being in each other’s shoes; that we are all connected, and that life has many surprises for us. My satisfaction comes from doing work that lifts others up and helps to support their dignity and importance in this world.

NS: I would say my feminist awakening was in residency. As a resident, I recall thinking, Well, I’m going to be an Ob/Gyn, so of course I’ll do abortions. Then I realized that not all Ob/Gyns offered them and that the whole topic was more complicated. I was very fortunate to have a fantastic mentor in residency – Tim Johnson, the chairman at Michigan – who encouraged my interest in Family Planning. I started working as an abortion provider at Planned Parenthood in my last years of residency, and my eyes were opened to the realities that women faced. One broken condom, one twist of fate, and a woman’s hopes, dreams and health could be at risk. During residency I was also incredibly impressed by the rigors of pregnancy, labor and the postpartum period, and found a lot of it risky and scary for my patients. I came to feel strongly that nobody should have to go through any of that
unless she is ready. I felt if my patient wants an abortion, somebody should do it for her, and that somebody should be me.

**Despite efforts to integrate abortion training into residency, it seems like the field of Family Planning is still marginalized in many parts of the country.**

AG: I had many colleagues tell me that it was a professional risk to pursue an area of medicine that has little support and is very misunderstood. Contraception, abortion and management of fetal deaths – these are not easy topics to discuss in casual conversations or hear about on the nightly news. But they are topics and situations that women find themselves dealing with every single day, and they are areas of reproductive health care where women struggle with decisions, carry shame that has been placed upon them by their families and societies, and where I felt I could be most helpful. I know that women are compassionate and thoughtful. I know that life is messy and unexpected. I know that women deserve compassion and respect as they face these choices and that they are often alone when they are faced with these choices.

NS: In the 1980s and 1990s, there was a significant segregation of where women got abortions: in separate clinics, outside of mainstream Ob/Gyn practice and outside of teaching hospitals. As a result, fewer Ob/Gyn residents were trained in how to prevent and perform abortions and to understand why women need them. The development of Family Planning as an academic subspecialty is part of the movement to integrate this important medical care for women into medical education and research. With this integration and normalization, we see a lessening of the stigma placed on women having abortions and the physicians who care for them.

**What do you think accounts for the segregation?**

NS: It’s multifactorial. If people aren’t trained in abortion provision, they’re not going to do it. If people aren’t taught about why it’s important, they might not feel motivated to overcome all the barriers to what it takes to provide abortions in their practice. Compared to other things that we can do as doctors, it doesn’t pay very well, so there’s also not much of a financial incentive. It also comes with a perception – and in many cases a reality – of harassment and even danger. So there are a lot of disincentives for physicians to include it as part of their regular practice.

AG: In the 1990s and early 2000s as I was entering medicine, there seemed to be an emphasis on conscience objection on the part of physicians, nurses, pharmacists, et al. While I certainly understand individuals’ decisions to opt out of abortion care, I similarly feel a very strong moral and ethical obligation to provide comprehensive reproductive health care for all women, including abortion care. And I think that emphasis on health care providers’ desires has unfortunately overshadowed our patients’ needs and therefore what health care they have available to them. Pregnant women desperate to end unwanted or unhealthy pregnancies don’t have the option of “opting out.”

But even the Accreditation Council for Graduate Medical Education (ACGME) requires that all Ob/Gyn residency programs include training in abortions. Why the need for specialty training in Family Planning? Why the need for a fellowship?

AG: Actually, the ACGME doesn’t stipulate that clinical training has to be given by the residency program. In my experience, getting training in second trimester abortion procedures was very difficult until I did a Family Planning fellowship. None of my attendings in residency regularly performed second trimester surgical abortions. Almost all of the pregnancy terminations performed at my training hospital were labor induction abortions. My program was supportive of me seeking that training elsewhere, and I arranged an elective to be trained in second trimester procedures with two local clinics. But when it came time for hands-on surgical experience, the individual physicians doing the
procedures were very wary to participate in training, given the medical/legal climate of Ob/Gyn in Philadelphia. I realized that if I wanted to offer my patients the best care – including surgical care of fetal demise in addition to labor induction – I needed to do the Family Planning fellowship.

NS: Of course, I think that abortion training in residency is very important. I ran the Ryan Program at the University of Rochester for 10 years and found my role in resident education to be very rewarding. But part of why I was seeking out new professional opportunities is that I really did want to build a fellowship program. First, there’s a different type of training you give to a fellow. You’re training that fellow for a subspecialty, for his or her chosen career. Second, the whole purpose of the fellowship program is to bring additional academic rigor to the research that’s done in the field. For far too long, abortion really was segregated out of academic medicine. It was a procedure very well done, very kindly done, but not necessarily with an eye toward improving best practices or researching patient preferences, best surgical techniques or providing this care from a health services model in a more effective way. That idea of striving to do better, being involved in research and helping to train people who want to do it — that’s what the fellowship uniquely offers.

I imagine it was a thrill to join Yale’s faculty.
What excited you most?

NS: I was recruited to Yale to bring my 10 years of experience in growing and running an excellent clinical and educational program in Family Planning with an eye toward building a fellowship program. And I feel very fortunate to partner with Aileen in this work. Given Yale’s rich legacy in advocacy for women’s health, the world-class research infrastructure and the innovative educational programs, I see this as fertile ground for the seeds we are planting. I am thrilled to dream big as we build the program here.

AG: I was recruited to join the faculty at Yale after finishing my Family Planning fellowship, and it has been a challenging and rewarding opportunity to build the Family Planning section from the ground up. When Nancy and I found out we were both interested in the position, we started phone dating. We realized that with two of us, there was a real opportunity to jumpstart something incredible at Yale, and that it would take two people to ramp up the clinical services, education for medical students and residents, and research portfolios. Given our complementary backgrounds, interests and skills, we were energized by the potential synergies we could bring. We’ve been here for about two and a half years. In my mind, we’re just getting started! Yale has opened doors to worlds that I didn’t even know existed. There is a rich legacy here of social justice, cutting-edge research and world-renowned education. Where else would you want to be?

What is a favorite moment of your day?

AG: Helping a patient smile. Exceeding her expectations. It always amazes me to hear patients say, “I didn’t think you’d be so nice!” That sentiment speaks volumes about how much women undervalue themselves and anticipate that they will be treated poorly. And I am happy to quell those expectations and give her new expectations of respect, kindness, compassion and excellent health care.

NS: Seeing a patient right before her abortion, putting her at ease. That moment you see the change in her body language, when she begins to relax and she realizes, OK, here’s someone who cares about me, who’s going to help me through this process, who’s going to give me excellent medical care. I’m not alone. It’s not going to be as scary as I thought. I really like being able to do that for my patients. Because I think women deserve deeply compassionate care when they’re going through something stressful — anything stressful — but this stress in particular because of the stigma that society places on women who have abortions. There’s a lot of shame and baggage that our patients are forced to carry, and I hope I can let them know that they don’t need to carry it with them when they come into my exam room.
What do you love most about our patient population?

AG: I think our patients are incredibly resilient.

NS: Yes, I think there are a lot of people out there with very challenging life situations, and I am continually impressed by their inner resources and their ability to live lives of meaning within situations that are difficult.

The 50th anniversary of Griswold v. Connecticut is next year, 2015. How do you plan to commemorate it?

NS: It’s an incredibly rich and important part of our history here at Yale, and it’s a history from which I draw inspiration – to remember that the chair of Yale Ob/Gyn felt it was so important to challenge what he thought was a medically unsound and socially unfair restriction that he deliberately broke the law and got himself arrested! Dr. Gariepy and I like to reassure Dr. Taylor that we are not planning to go out there and get arrested. But the degree of that commitment is really inspirational. The huge transitions that have happened across our society in the past 49 years – for women and women’s health and access to contraception – are really something to celebrate. There’s a good argument to be made that contraception is the biggest public health success story of the 20th century; it has transformed societies by allowing women to have the children they want to have when they want to have them. We know that when women around the globe have access to contraception, they are healthier, their children are healthier, their families are healthier and societies all rise together. So I think the 50th anniversary is a great time to draw inspiration anew and to look forward to our next chapter in Family Planning at Yale.

AG: I would love to celebrate Dr. Buxton by endowing a Chair of Family Planning at Yale in his name. That is how I’d like to commemorate the 50th anniversary of Griswold v. Connecticut! What a way to celebrate a legacy and ensure that Yale remains on the forefront of Family Planning for years to come.

What are you most excited about for Yale Family Planning?

NS: We both came to Yale with the goal of establishing Yale as a site for the Fellowship in Family Planning. We’ve worked on our program and our application for three years. Just this month we learned that we have been awarded the Fellowship. We are thrilled for this milestone and look forward to training the next generation of leadership in Family Planning here at Yale.

AG: I agree. I think the approval to start a Yale Fellowship in Family Planning is incredibly exciting! Yale is the 29th Fellowship in Family Planning site in the U.S., and we know that the bounty of resources we have at Yale for a clinical training, research, and advocacy will make us a very competitive site. Yale’s first Family Planning Fellow will start in 2015. That sounds like the perfect way to commemorate the 50th anniversary of Griswold v Connecticut!

Abby Cutler, MD, is a first-year Ob/Gyn resident. Her writing has appeared in The Atlantic and The Christian Science Monitor.
Reproductive Health in Our Backyard:
A Timeline

1879: Connecticut Legislature passes a statute on birth control, forbidding the use of drugs or instruments to prevent contraception.

1923: The Connecticut Birth Control League is formed.


1939: Two physicians and a nurse are arrested at a Waterbury clinic, prompting other clinics around the state to shut down.

1940s: Multiple lawsuits are filed by physicians in an effort to change state law. All fail.

1950s: Planned Parenthood (formerly the Connecticut Birth Control League) buses women from Connecticut to New York and Rhode Island, where they can obtain contraception.

1960: The Supreme Court rejects yet another Connecticut lawsuit, citing the archaic law as “dead words and empty shadows.”

1961: Executive Director of Planned Parenthood Estelle Griswold and Yale Chair of Ob/Gyn C. Lee Buxton test this by opening a birth control clinic in New Haven with the hopes of being arrested. They are successful. Planned Parenthood brings the case to the Supreme Court, and it is argued by Dean of Yale Law School Thomas Emerson.

1965: The Supreme Court strikes down Connecticut’s birth control law in Griswold v. Connecticut on the basis that it invades the privacy of individuals, becoming the basis for subsequent decisions on reproductive rights such as Roe v. Wade.

1960s-1970s: Abortions and sterilizations are provided at Yale via therapeutic abortion committees (TACs), which grant permission on a case-by-case basis depending on the “medical or psychiatric indications” for the procedure.


1975: A group of young women from Yale Law School helps found Women’s Health Services, a freestanding abortion clinic that initially operates out of the private office of Dr. Virginia Stuermer, a Yale Ob/Gyn faculty member.

1999: The Ryan Program is created at UCSF with the goal of integrating and enhancing Family Planning training for obstetrics and gynecology residents in the United States and Canada.

2005: Yale receives a Ryan Grant and creates its first dedicated rotation in Family Planning.
Pediatric Gynecology – Birth Through Adolescence

INTRODUCTION

Contrary to popular belief, there are many gynecologic needs that arise within the pediatric population. These include monitoring for normal pubertal development, diagnosing congenital anomalies, diagnosing menstrual disorders, offering anticipatory guidance for sexual health (including HPV vaccine counseling, education about date rape and contraceptive counseling), performing pelvic exams in select circumstances, discussing healthy eating habits, discussing safety and injury prevention, managing gynecologic complications of chronic illnesses and diagnosing the rare pediatric gynecologic neoplasm.

Children are not just smaller versions of adults, but rather present with different physiological, developmental and emotional needs. As children progress from childhood through adolescence, there is an evolving independence, coupled with fear and embarrassment over their ever-changing bodies. There often is an interaction between their stage of development and various disease processes. There exist some unique health issues within the pediatric population. As health care providers, we also have unique opportunities to potentially prevent adult diseases.

Due to their development, children present with vulnerabilities to health problems, especially as they relate to risk-taking behaviors. When dealing with pediatric patients, it is important to know the confidentiality requirements, which vary depending upon where you practice. Due to all of these features, there is a growing subspecialty within the field of obstetrics and gynecology known as PAG (pediatric and adolescent gynecology). Currently, there are nine PAG fellowships throughout the United States and Canada, the first founded in 1986.

CONFIDENTIAL GYNECOLOGIC CARE AND THE ADOLESCENT IN CONNECTICUT

The confidentiality laws with regard to gynecologic care change over time and can be accessed easily online at www.guttmacher.org, which is updated monthly. In Connecticut, adolescents may receive confidential care and do not require parental permission or notification for the following: sexually transmitted infection (STI) diagnosis and treatment (including HIV, but must be reported if a child under 12 years has an STI); contraceptive care (including emergency contraception if the minor is married or receiving care at a Title X clinic); pregnancy-related care (including termination of pregnancy, although Connecticut has no explicit policy regarding termination of pregnancy in minors); drug and alcohol addiction treatment; mental health services (for up to six visits, after which parental permission is required); and emergency or life-threatening situations.

PEDIATRIC GYNECOLOGIC VISIT AND EXAM

The first gynecologic exam should take place between the ages of 13 and 15. Most often, a pelvic exam need not be done, unless indicated...
by symptoms or disease. At this time, the gynecologist can begin to establish trust, build the physician-patient relationship and offer guidance, screening and preventive care. If the adolescent is sexually active, STI screening can be done; this need not always require a speculum exam, as nucleic acid tests for chlamydia and gonorrhea can be done on urine, and other STIs require serum. The first Pap smear is now not done until age 21, with limited exceptions.

When examining a PAG patient, it is important to explain that the exam is sanctioned by their caregivers and to differentiate it from other types of “touches.” When a child is under 14 years, she is examined with a caregiver present. When a child is 14 and older, she is given the choice of being examined by herself or with a caregiver present. Positioning of the child for a gynecologic exam is not routinely done in the dorsal lithotomy position with her legs in footholds, as we do for adults. Often, visualization is aided with the child positioned supine with legs frog-legged or knees flexed on the abdomen, which can be on a table or on a caregiver’s lap. For younger children, the knee-chest, face-down position is useful (like the child’s pose in yoga). While office pelvic or speculum exams prepubertally are ill advised, a rectoabdominal exam can confirm the presence of a uterus, and an abdominal exam can often palpate enlarged ovaries.

One useful technique when examining the PAG patient is the lateral spread technique, whereby the physician’s thumb and index finger are used to grasp the posterior labia majora and apply lateral and outward traction; this greatly aids in visualization of the hymen. Another useful technique is vaginal lavage with the “catheter in catheter” method described by Pokorny. This method can be used to irrigate out a vaginal foreign body or to collect a specimen for cytology, wet mount or cultures. For this technique, a proximal IV catheter (without the needle) is placed inside the distal four inches of a number 12 red rubber catheter, which is placed in the vagina, and about 0.5 to 3 ml of saline are then flushed into and removed from the vagina. Moistened male urethral swabs can also be placed inside the introitus for culture or cytology. Additionally, vaginoscopy is an excellent adjunct for PAG patients, and this can sometimes be accomplished in the office. When performing vaginoscopy, it is important to remember that the prepubescent cervix is the same color and texture as the vagina, and is typically flush with the vaginal vault.

Next we will discuss common PAG gynecologic issues within different PAG populations.

**COMMON PAG ISSUES IN THE NEONATAL POPULATION**

Thankfully, there are not many gynecologic problems during the neonatal period. All neonates should have an evaluation of the breasts and external genitalia before being discharged from the hospital. Breast buds, nipple discharge and white vaginal discharge are common and result from exposure to maternal estrogens *in utero*. Most of these changes should resolve within two weeks, although breast buds may persist for up to two months. Some neonates experience a small amount of vaginal bleeding as a result of withdrawal from maternal estrogens. While this is often anxiety provoking for parents, if found within the first 10 days of life, you can offer reassurance of nothing pathologic.

The external genitalia always should be examined at birth; if they are ambiguous, no gender should be assigned to the child, and the parents should be informed that the genitalia are “incompletely formed.” It is most important to evaluate for congenital adrenal hyperplasia, primarily 21-hydroxylase deficiency, which can be life threatening soon after birth in its salt-wasting form, which accounts for 90% of cases. If clitoral enlargement is questioned, a clitoral index can be measured (glans length by width in mm$^2$), and if greater than 5 mm$^2$, congenital adrenal hyperplasia should be ruled out. The term to be used for disorders where chromosomal, gonadal and anatomic sex are atypical and not in synchrony is Disorders of Sexual Differentiation (DSDs). Patient hymen is also easy to determine before the newborn leaves the hospital, as
whenever the newborn cries, the doctor uses the Valsalva maneuver to make the hymen easy to see.

Another neonatal gynecologic problem is ovarian cysts, which are symptomatic in 1/2500 live births. Most of these cysts are simple and resolve spontaneously. As malignancy is rare, conservative management is best, and intervention need only be considered if the cyst is over 5 cm, complex or causing pain.

COMMON PAG ISSUES IN THE PEDIATRIC POPULATION (1–9 YEARS)

VULVOVAGINITIS

Vulvovaginitis is an inflammation of the vulvar and vaginal tissues, and is the most common prepubertal gynecologic complaint. Pediatric patients have many factors that put them at risk, including anatomic factors (lack of pubic hair, no labial fat pads, proximity of the vagina to the rectum), poor hygiene (bathroom hygiene of not wiping only front to back, wearing diapers), hormonal status (lack of estrogen causes a thin, atrophic vagina with a basic pH of 6.5–7.5) and if they have other predisposing conditions (such as diabetes, obesity, vulvar dermatoses, immune disorders). It is important to differentiate this from normal discharge, such as that associated with estrogen exposure of either the neonate (see above) or of the premenarchal girl after thelarche. Vaginal discharge affects 50% of PAG patients with vulvovaginitis, but other presenting symptoms include dysuria, pruritus, pain, genital irritation, erythema and excoriations from scratching. It is important to ask about symptom duration, color, bathroom hygiene technique, bedwetting, medications and irritants (such as bubble baths and soap).

The most common etiology is nonspecific vulvovaginitis, which accounts for 70% of premenarchal vulvovaginitis, is secondary to urinary/fecal hygiene and is caused by mixed bacteria of enteric, respiratory and/or skin origin. Pinworm can be a cause of pediatric vulvovaginitis, but rarely is candida a cause in children over 2 years, as candida tends to grow in more acidic environments, like in the adult vagina with its pH of 3.8–4.5. Sexual abuse should be investigated if the vulvovaginitis is caused by Neisseria gonorrhoeae or Chlamydia trachomatis, or if a wet mount reveals abundant white cells, clue cells or bacteria. Treatment mostly involves hygiene measures and avoiding irritants, unless a specific pathogen is identified.

VULVAR DISORDERS

Candidiasis, or diaper rash, in children under 2 is a common pediatric vulvar disorder. Molluscum contagiosum, which causes smooth papules with a central umbilication and “cheesy” plug, can be found on any skin surface, and is most often not from sexual contact. Genital warts, or condyloma accuminata, are caused by the human papilloma virus (HPV), especially types 6 and 11, which account for 90% of genital warts. Any skin-to-skin contact can spread HPV, and it is important to realize that it occurs mostly due to perinatal transmission of HPV acquired during passage through the birth canal in young children. One should not suspect sexual abuse unless the child is presenting with lesions starting after age 2 or 3, at which point sexual abuse should be ruled out as perinatal transmission is less likely. Both molluscum contagiosum and condyloma accuminata are self-limited conditions without oncogenic potential, so often no treatment is necessary. If molluscum contagiosum causes pain or embarrassment or gets secondarily infected, it can be treated with a variety of desiccants. If condyloma accuminata gets very large or obstructs the urethra, causing urinary retention, it can be treated with any adult treatment, although none are FDA approved in the pediatric population.

LABIAL AGGLUTINATION

Labial agglutination is when the adjacent edges of the labia minora adhere to one another, and it starts posteriorly. Patients present with parents saying that they can’t see their daughter’s vagina, and a clinical exam pearl is to follow the labia minora. It is caused by low estrogen levels coupled with inflammation. Treatment is mostly hygiene based with or without estrogen cream.
There is no impact on puberty, growth, sexual function or future fertility. Only in severe cases, such as those complicated by urinary retention, is surgical mechanical separation required.

**VAGINAL BLEEDING**

Vaginal bleeding is always important and requires evaluation in a pediatric patient. History should be obtained regarding growth, pubertal milestones, household medications (such as oral contraceptive pills or cosmetics, which sometimes contain estrogenic substances), trauma, prior vaginal foreign bodies (which tend to be recurrent) and red flags for sexual abuse. It’s important to determine the source of the bleeding as vulvar, vaginal or endometrial, although endometrial bleeding is rare in premenarchal girls. Other sources include urologic.

The most common causes of vaginal bleeding in pediatric patients are inflammatory, with vulvovaginitis being the most common. Sexually transmitted infections are a potential, but infrequent, cause of vaginal bleeding. Parasites such as shigella can cause bloody vaginitis, and only 20% of the time is shigella associated with diarrhea. Trauma is a frequent cause of bleeding, and it is important to exclude sexual abuse (for more on sexual abuse, see below). It is important to assess if the history of trauma is compatible with the injury seen, but straddle injuries are common, as are vaginal foreign bodies. Many different objects have been found as vaginal foreign bodies in children, but small pieces of toilet paper are the most frequent. These are associated with vaginal bleeding from irritation and often a secondary vulvovaginitis. Hormonal causes of vaginal bleeding, while less common, can be due to exogenous hormones (such as oral contraceptive pills, which look like candies), sex hormone tumors (ovarian or adrenal origin) or precocious puberty (with causes that include idiopathic, brain tumors and McCune-Albright syndrome). Urologic tract bleeding can be confused for vaginal bleeding, and urologic sources include urethral prolapse, urinary tract infections, hematuria and urologic neoplasms.

Vulvar lesions may also bleed, such as large condyloma accuminata or lichen sclerosus. In lichen sclerosus, flat, ivory-colored papules may coalesce into plaques in a keyhole distribution around the introitus and anus, and cause itching. They can even present with purpura, erosions and fissures, which can be wrongly mistaken for sexual abuse. The prognosis is good if treated promptly with potent steroids, but if left untreated permanent scarring and impaired sexual function can ensue. Tumors are thankfully rare, but ovarian germ cell tumors (which produce estrogen) and vaginal embryonic rhabdomyosarcoma (also known as sarcoma botryoides) may both present with prepubertal vaginal bleeding.

**SEXUAL ABUSE**

The term “sexual assault” refers to attempted sexual touching of another person without their consent and includes sexual intercourse (rape), sodomy (oral-genital or anal-genital contact) and fondling. The term “sexual abuse” refers to when a child engages in sexual activity for which he/she cannot give consent, and includes sexual assault plus non-touching abuses such as exhibitionism, voyeurism or involving the child in pornography. This is to be differentiated from “sexual play,” which is considered normal, and involves children of the same age or developmental level who engage in non-coerced viewing or touching of each other’s genitalia because of mutual interest or curiosity. Sexual play does not have the psychological, developmental or physical consequences that sexual abuse has. About 1% of children in the United States are abused sexually each year, and worldwide 25% of girls and 9% of boys are sexually abused.

Findings suspicious for sexual abuse of a girl include sexual precocity, a history of vaginal trauma not compatible with the injury found, or certain STIs. Wet mounts or vaginal cultures positive for the following infections should prompt investigations for abuse: trichomoniasis, chlamydia in a child over 18 months (ruling out perinatal transmission), condyloma acumínata
onset in a child over 2 or 3 years (unlikely to be perinatal transmission) and gonorrhea. No findings on physical exam are diagnostic for abuse, but the following exam findings arouse suspicion for abuse: posterior hymenal lacerations or transections and hymenal caruncles that can be associated with nontreated, severe stretch injuries. Oftentimes, sexual abuse leaves no visible injuries.

Signs of sexual abuse and sexually transmitted infections in children must be reported to protective service agencies, and providers need to be aware of the laws in their state. Forensic evidence should be collected within 72 hours. To address both short-term emotional needs and long-term sequelae, referrals to social workers or mental health professionals should be made. If risk exists for hepatitis B, hepatitis C or HIV, prophylaxis should be given, while chlamydia and gonorrhea prophylaxis need not be given as those infections are rare to contract in the pediatric population.

COMMON PAG ISSUES IN THE EARLY ADOLESCENT POPULATION (10–13 YEARS)

As puberty most commonly occurs during this age group, many congenital reproductive tract anomalies and menstrual disorders may present. Congenital anomalies may present as menstrual disorders concurrent with menarche. Dysmenorrhea since menarche should raise suspicion for a partial outflow tract obstruction, while primary amenorrhea after otherwise normal pubertal development should raise suspicion for an obstructive anomaly. Obstructive anomalies can be of either Müllerian (such as Müllerian agenesis or transverse vaginal septum) or urogenital sinus (such as imperforate hymen) origin. If menstrual outflow is prevented, there is increased retrograde menstruation and increased resultant incidence of endometriosis.

Dysmenorrhea occurs in as many as 50% to 70% of girls. For girls with menstrual cycle abnormalities, a detailed history is paramount. One should look for stigmata of genetic diseases, like Turner Syndrome, and for psychosocial issues, like stress, excessive exercise and eating disorders. The majority of girls will establish menstrual cyclicity within six to 12 months, and persistent oligomenorrhea may predict lifelong irregular cycles. According to research by Ibnez, of those girls oligomenorrheic at age 15, 50% of them remain oligomenorrheic at age 18. Recognizing this may lead to early diagnosis of polycystic ovarian syndrome (PCOS) and potentially PCOS-preventive treatments in the future. It should be noted that there are currently no definitive adolescent PCOS diagnostic criteria. Some authorities recommend utilizing all three Rotterdam criteria in making a PCOS diagnosis in adolescents, as well as ensuring the adolescent is at least two years out from menarche. For more information, refer to the 2012 ESHRE/ASRM-sponsored Third PCOS Workshop Group Consensus.

COMMON PAG ISSUES IN THE MIDDLE ADOLESCENT POPULATION (14–17 YEARS)

The middle adolescent continues to develop both physically and psychosocially. Physically, there is a maturation of menstrual cycles, linear growth completion and weight gain. Psychosocially, there exists increased body consciousness, greater strained family communications, high levels of stress, higher risks for depression, emerging sexuality and initiation of risk behaviors. The frontal lobe of the brain, which helps us to understand there are consequences to our actions, is not fully developed until late into our 20s, and may play a role in why teens engage in higher rates of risk behaviors. The Centers
for Disease Control has conducted a Youth Risk Behavior Surveillance Survey biannually since 1991, which consists of a 95-question in-school survey and provides data on health-risk behaviors among ninth- to 12th-grade students in the United States. Data is collected from private and public schools from all over the country (collected by state, territorial, tribal and local education and health agencies), includes data from all socioeconomic groups and is ethnically diverse. Risk behaviors assessed include sexual behaviors, drug- and alcohol-related behaviors and behaviors related to violence. What is clear is that United States high school girls (from diverse socioeconomic, ethnic and geographic groups) are engaging in sex, using drugs and drinking alcohol at significant rates. By age 19, as many as 85% of girls have engaged in some form of sexual contact (vaginal, anal, oral or same-sex).

Sexuality trends over the last century include a younger age of menarche and fertility (partially due to better nutrition and health care), younger age of coitarche (with less parental supervision as more homes have two working parents and more media influence) and older age of marriage (with longer education and fewer legal and religious controls). Along with these changes in sexuality trends come increases in teen pregnancy rates. About 8% of 15–19-year-old United States girls have been pregnant, making the teen pregnancy rate higher than in any other industrialized country. Of those teen pregnancies, 60% end in live births, 30% end in abortions and 10% end in miscarriages. One fifth of the abortions in the United States are performed on women under 19 years of age. In addition to higher teen pregnancy rates, these sexuality trends also come with risks for STIs. Contracting an STI is three times more likely to occur in teen girls versus 25–29-year-old women, likely related to both biological and behavioral risk factors. In addition, 11% of sexually active girls have asymptomatic chlamydia cervicitis, which progresses to pelvic inflammatory disease 15%–40% of the time. Moreover, if chlamydia cervicitis is treated, progression to pelvic inflammatory disease is reduced by 56%.

The middle adolescent years offer opportunities for counseling regarding contraception, safe sex practices, options if pregnant, date rape (and the power of their refusal), responsible socialization (designated drivers) and healthy eating habits. While gynecologists don’t routinely give vaccinations, it is important to make sure that our adolescent patients have been offered both the HPV vaccine series and the meningococcal vaccine booster.

In conclusion, PAG patients are a vulnerable population who present with unique opportunities for prevention. We can diagnose, treat and prevent STIs, perform Pap smears from age 21 on and diagnose common disorders (as discussed above). During this time period, reproductive anomalies often present themselves. If we are lucky, we may help shepherd this population safely to adulthood.
REFERENCES


Impact of Body Mass Index on Surgical Outcomes and Analysis of Disease Recurrence for Endometrial Cancer Patients Undergoing Robotic-Assisted Staging

OBJECTIVE

To evaluate the impact of body mass index (BMI) on the short- and long-term outcomes of endometrial cancer patients who underwent robotic-assisted staging, and to analyze disease recurrence and recurrence-free survival (RFS).

MATERIALS AND METHODS

The charts of all consecutive patients with endometrial cancer who underwent robotic surgery from March 2007 to October 2012 were analyzed. Patients with follow-up less than 12 months after surgery were censored from the RFS analysis.

RESULTS

Mean age for the 364 patients was 63.6±10 years and BMI was 34.8±10.1 kg/m². Conversions were in 3/364 cases (0.8%). The mean operative time was 162.3±54.6 min. Postoperative hospitalization was 1.62±1.93 days. Histology included 80.8% endometrioid and 19.2% clear cell, serous and carcinosarcomas. Mean pelvic and para-aortic lymph node counts were 15.9±8.2 and 3.6±4.3, respectively. Metastatic disease was diagnosed in 58/364 (16%) patients, and lymph node metastases only were identified in 30/364 (8.2%) patients. There were 98/364 patients (26.9%) who received no adjuvant treatments, brachytherapy only was administered to 169/364 patients (46.5%), and 94/364 patients (25.8%) were treated with chemotherapy. The median follow-up was 29.3 months. The recurrence rates were 4.1% for patients with endometrioid carcinoma and 14.1% for non-endometrioid histologies. Increasing BMI did not adversely affect the operative outcomes, and the recurrence rates were lower with higher BMI. The three-year overall survival was 98.2%, and the three-year RFS was 92%.

CONCLUSIONS

Recurrence rates for endometrioid, serous, clear cell carcinomas and carcinosarcomas were higher for all patients with BMI<30 kg/m² compared to BMI>30 kg/m².

INTRODUCTION

The prevalence of obesity in North America has increased steadily over the last decades and is now considered endemic with significant health implications (1). In 1960, 44% of U.S. adults were overweight or obese. This percentage has risen to 68.8% in 2010. Of these, 6.3% were morbidly obese. Should current trends continue, 75% of adults in the United States are projected to be overweight and 41% obese by 2015 (2). Once common in developed countries, obesity is now a worldwide epidemic. More than 1.4 billion adults worldwide were overweight in 2008, and more than 0.5 billion obese (3).

The association between obesity and endometrial cancer is well documented (4-8). With an
estimated 49,560 new cancer cases of the uterine corpus expected to be diagnosed in 2013, causing an estimated 8,190 deaths, uterine cancer is the fourth most common cancer and eighth most common cause of cancer death among women in the United States (9). Surgery is the mainstay in the treatment of uterine cancer. The majority of gynecologic oncologists use the robotic system for surgical staging in patients with uterine malignancies (10, 11).

The aims of this study were to evaluate short- and long-term outcomes of endometrial cancer patients who underwent robotic surgery at our institution and to analyze how obesity impacts treatment, disease recurrence and overall survival.

**MATERIALS AND METHODS**

This retrospective study was approved by the Institutional Review Board, which waived the informed consent requirement. The medical records were reviewed for all patients who underwent robotic surgery for endometrial cancer from March 2007 to October 2012. Information recorded included the patients’ demographics data, medical history, operative and anesthesia records, pathology and imaging studies, follow-up data, and the times to recurrence and overall survival where applicable.

Operative time was defined as the interval from skin incision to port closure. Recurrence-free survival (RFS) was defined as the time from surgery to the date of first recurrence. Overall survival (OS) was defined as the time from surgery to the date of death or date of the last follow-up. Patients lost to follow-up were censored at their last date of contact.

The staging used in this study was according to the FIGO 2009 criteria (12). Short-term postoperative outcomes and complications were defined as those occurring within 30 days of surgery, and long-term complications were considered as those occurring later than 30 days.

The patients were consecutively scheduled for robotic surgery, regardless of body habitus or number of previous surgeries. The patients were operated by laparotomy when they presented with upper abdominal metastases. Pelvic metastatic disease or pelvic and/or para-aortic lymphadenopathy was not a contraindication to the robotic approach. Upper abdominal recurrences, when limited, were also approached robotically. All cases were operated using a five-port/four-arm technique. A uterine manipulator or sponge stick was used according to the surgeon’s preference. The manipulator was inserted after peritoneal washings were obtained to prevent contamination of the cytology specimen. The operative techniques have been previously described (13-15).

Uteri too large for intact transvaginal delivery were removed from the peritoneal cavity via small laparotomy at the completion of the case. In addition to pelvic and para-aortic lymphadenectomy, infracolic omentectomy was part of the surgical staging in patients with serous carcinoma, clear cell carcinoma and carcinosarcomas. Fellows or residents were involved in all cases. In 60% of cases, they sat at the console for a minimum of 30 minutes and performed at least the vaginal apex closure.

The institutional protocol for patients with endometrioid carcinoma is brachytherapy to the vaginal apex for all patients with the exception of stage IA, G1, less than 10% myometrial invasion and no lympho-vascular invasion (LVI). In addition, chemotherapy is added for stages III and IV and for stages I and II with positive peritoneal cytology. The institutional protocol for all patients with uterine serous carcinoma, clear cell carcinosarcomas and carcinosarcomas is combination chemotherapy and vaginal brachytherapy regardless of the stage with the exception of the following clinical situation: stage IA with no residual tumor in the hysterectomy specimen and negative peritoneal cytology (16, 17). The most common combination chemotherapy was carboplatin AUC=5 and paclitaxel 175 mg/m² administered every 21 days times six cycles. The radiotherapy dose was 2100 cGy administered in three fractions, one week apart for brachytherapy alone and
1400 cGy in two fractions when combined with chemotherapy.

Follow-up after completion of treatment was every three months for two years, then every six months for another three years. For patients with type II cancers or endometrioid cancers with metastases or positive peritoneal cytology, CA-125 levels were also drawn at follow-up visits.

Statistical analysis was performed using either the generalized linear model (GLM) or Wilcoxon rank sum test for numerical variables. For categorical variables, Chi-square or Fisher’s exact test was carried out. Multivariable regression analysis was performed with the Cox proportional hazards model. Kaplan-Meier survival curves were graphed to estimate overall survival and recurrence-free survival. Log-rank tests were performed to examine unadjusted differences in survival by BMI category and histology. Subjects were excluded from the analysis of recurrence-free survival if they had less than 12 months of follow-up unless they recurred within the first 12 months.

RESULTS

Three hundred sixty-four patients underwent robotic surgery for endometrial cancer at our institution from March 2007 to October 2012. The mean patient’s age was 63.6±10 years (range 39-91) and the mean BMI was 34.8±10.1 kg/m² (range 17.5-94). The procedure was completed by laparotomy in 3/364 (0.8%) cases. The mean operative time was 162.3±54.6 min., and estimated blood loss (EBL) was 114±101 mL (range 25-600). The mean specimen weight was 158 grams (range 31-1048). Length of postoperative stay was 1.62±1.93 days (range 0-22).

Lymphadenectomy was not performed in 20/364 patients (5.5%). In 19/20 patients, the pre- and intraoperative pathological evaluations were consistent with endometrial atypical hyperplasia. Postoperatively, the paraffin sections identified carcinoma. All these tumors were of low architectural grade and minimally invasive or with no myometrial invasion. None of these patients were diagnosed with recurrence with a mean follow-up of 50 months (range 24-82). In 1/20 patients with undifferentiated endometrial sarcoma, lymphadenectomy and omentectomy were omitted because of intraoperative disseminated intravascular coagulation. After her postoperative recovery, this patient was lost to follow-up and was censored.

<table>
<thead>
<tr>
<th>TABLE 1: PREOPERATIVE CHARACTERISTICS AND OPERATIVE RESULTS OF PATIENTS WHO UNDERWENT ROBOTIC-ASSISTED STAGING FOR ENDOMETRIAL CANCER</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGE (n=364)</td>
</tr>
<tr>
<td>BMI (n=364)</td>
</tr>
<tr>
<td>TOTAL NODES (n=364)</td>
</tr>
<tr>
<td>PELVIC NODES (n=364)</td>
</tr>
<tr>
<td>PARA-AORTIC NODES (n=261)</td>
</tr>
<tr>
<td>OPERATIVE TIME (n=364)</td>
</tr>
<tr>
<td>EBL (n=364)</td>
</tr>
<tr>
<td>LOS (n=364)</td>
</tr>
<tr>
<td>HISTOLOGY</td>
</tr>
<tr>
<td>STAGE</td>
</tr>
<tr>
<td>GRADE</td>
</tr>
<tr>
<td>ADJUNCT TREATMENTS</td>
</tr>
<tr>
<td>LN METASTASES (n=36)</td>
</tr>
</tbody>
</table>

Pelvic lymphadenectomy only was performed in 344/364 (94.5%) patients, and pelvic and para-aortic lymphadenectomy was performed in 261/364 (71.7%) patients [Table 1].
The mean number of pelvic and para-aortic lymph nodes excised was 15.9±8.2 and 3.6±4.3, respectively. Lymph node metastases were diagnosed in 30/364 (8.24%) patients. Of these, in 20/364 (5.49%) only the pelvic lymph nodes, in 3/364 (0.82%) only the para-aortic lymph nodes and in 7/364 (1.92%) both the pelvic and para-aortic lymph nodes were involved with disease. The histology of these metastatic tumors is shown in Table 1.

Fifty-eight/364 patients (16%) were diagnosed with metastatic disease. All visible lymphadenopathy or gross intraperitoneal disease was resected to no visible residual tumor.

Intraoperatively, the following inadvertent injuries occurred: one to a major vessel, three to the bowel, three to the ureter and four to the bladder. The external iliac vein was injured with the tenaculum transvaginally in one patient when retrieving the specimen, and hemostasis and repair were performed robotically. Three enterotomies and four cystotomies were recognized intraoperatively and repaired robotically. Three ureteral injuries were diagnosed in the postoperative period.

The most significant event recorded in the postoperative period was the death of an 85-year-old with preexisting cardiac disease. The patient developed a myocardial infarction and pulmonary edema on POD 2 and declined cardiopulmonary life support. Three/364 patients (0.8%) developed an ileus, and 3/364 patients (0.8%) returned with vaginal apex dehiscence requiring operative repair. Six/364 patients (1.6%) were diagnosed with venous thromboembolism. Eighteen/364 patients (4.9%) were readmitted within the first 30 days and 28/364 (7.7%) within the first 90 days [Table 2].

Endometrioid histology was diagnosed in 293/364 (80.8%) tumors. Grade 1 was the most common (40.7%), followed by grade 2 (39.4%) and grade 3 (19.9%). Uterine serous carcinoma was diagnosed in 47/364 patients (12.9%), carcinosarcoma was present in 14/364 patients (3.6%), sarcoma in 6/364 patients (1.6%) and clear cell carcinoma in four patients (1.1%) [Table 1]. The stage distribution is detailed in Table 1.

Ninety-eight/364 patients (26.9%) did not receive any adjuvant treatment. Adjuvant therapy was not indicated for 78/98 patients, and 20/98 patients declined therapy. Brachytherapy only was administered to 169/364 patients (46.5%). Three/364 (0.8%) patients were treated with pelvic external beam therapy and brachytherapy. Ninety-four/364 patients (25.8%) were treated with chemotherapy [Table 1]. Of the 293 patients with endometrioid histology, 89/293 patients (28.3%) received no treatment after surgery, 165 patients (56.3%) were treated with vaginal apex brachytherapy, and 39 patients were treated with chemotherapy with or without radiation.

The median follow-up time was 29.3 months (interquartile range: 15.6-43.1). During this time, 22/364 patients (6%) were diagnosed with recurrence of disease. The recurrence rates were 4.1% for patients with endometrioid carcinoma and 14.1% for non-endometrioid histologies. Recurrences of uterine serous carcinoma, clear cell carcinoma and carcinosarcomas were diagnosed in 10/22 patients (45.5%), whereas 12/22 patients (54.5%) had endometrioid histology. Sites of first recurrence for patients with endometrioid carcinomas were vaginal apex in two cases, pelvis in one case, retroperitoneal in three cases and multiple sites in six cases.

| TABLE 2: INTRAOPERATIVE AND POSTOPERATIVE COMPLICATIONS |
|------------------------------------------|-------|
| INTRAOPERATIVE COMPLICATIONS             | n    | %   |
| Conversion                               | 3    | 0.8 |
| Vessel injury                            | 1    | 0.3 |
| Bowel injury                             | 3    | 0.8 |
| Ureteral injury                          | 3    | 0.8 |
| Bladder injury                           | 4    | 1.1 |
| Transfusion                              | 0    | 0.0 |
| Neurologic comp                          | 0    | 0.0 |
| Cardiopulmonary                          | 0    | 0.0 |

<table>
<thead>
<tr>
<th>POSTOPERATIVE COMPLICATIONS</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transfusion</td>
<td>12</td>
<td>3.3</td>
</tr>
<tr>
<td>Ileus</td>
<td>3</td>
<td>0.8</td>
</tr>
<tr>
<td>Cuff dehiscence</td>
<td>3</td>
<td>0.8</td>
</tr>
<tr>
<td>Pelvic fluid collection/abdominal-pelvic abscess</td>
<td>9</td>
<td>2.5</td>
</tr>
<tr>
<td>Lymphedema</td>
<td>14</td>
<td>3.8</td>
</tr>
<tr>
<td>VTE</td>
<td>6</td>
<td>1.6</td>
</tr>
<tr>
<td>Urinary complications</td>
<td>17</td>
<td>4.7</td>
</tr>
<tr>
<td>Cardiac/pulmonary complications</td>
<td>24</td>
<td>6.6</td>
</tr>
<tr>
<td>Death</td>
<td>1</td>
<td>0.3</td>
</tr>
<tr>
<td>Readmission</td>
<td>18</td>
<td>4.9</td>
</tr>
<tr>
<td>Neuropathies</td>
<td>9</td>
<td>2.5</td>
</tr>
<tr>
<td>Fever/neutropenia of unknown origin</td>
<td>33</td>
<td>5.1</td>
</tr>
</tbody>
</table>
[Table 3]. There were no port site metastases. Three/22 (13.6%) of all patients who recurred are dead of disease (DOD), 13/22 (59%) were alive with disease (AWD) and 6/22 (27.4%) were alive with no evidence of disease (NED) at the end of the follow-up. The six patients who are alive with NED after recurrence had endometrioid tumors. Three had stage I and II disease with no adjuvant brachytherapy and recurrence at the apex; they were treated with pelvic external beam radiation and were NED after 14-16 months. Three patients had stage III disease with recurrences in lungs or retroperitoneum; they were treated with systemic therapy +/- resection and were NED after 36-57 months.

In order to estimate the adequacy of surgical staging, we surveyed the 255/364 patients with stage I and II endometrioid disease who relapsed in the retroperitoneum. We found 1/255 (0.4%) stage IIA patient who recurred in the vaginal apex and retroperitoneum after surgery with 22 lymph nodes removed. Postsurgical adjuvant therapies were declined on account of the age of 90 years.

We sought to determine whether obesity impacts the surgical outcomes of endometrial cancer patients who underwent robotic surgery. Patients were categorized into four different BMI groups: <30, 30-39.9, 40-49.9 and >50 kg/m². The short-term outcomes analyzed were operative time, conversion rate to laparotomy, intraoperative complications, EBL, LOS and readmissions within 30 days from surgery [Table 4]. Statistically significant results were observed for LOS and EBL. Conversion rates were too low to reach a difference between categories.

The disease status was analyzed for the BMI categories listed above. Recurrences were diagnosed in 15/125 patients (12%) with BMI<30 kg/m², 4/135 patients (2.9%) with BMI 30-39.99 kg/m², 2/76 patients (2.6%) with BMI 40-49.99 kg/m² and 1/28 patients (3.6%) with BMI>50 kg/m². The recurrences followed a reverse trend with increasing BMI. Most recurrences (15/22, 68.2%) occurred in patients with BMI<30 kg/m². Recurrences in obese patients were 7/22 (31.8%) patients (3/22, 13.6% in morbidly obese patients). Patients with BMI <30 kg/m² had higher recurrence rates for all histologies when compared to patients with BMI >30 kg/m² [Table 5].

The patients included in this study had a three-year overall survival of 98.2% and a three-year recurrence-free survival of 92%.

**DISCUSSION**

In the United States, the robotic system has become the main laparoscopic tool in the treatment of endometrial cancer (11). Multiple studies have analyzed the outcomes of uterine cancer patients undergoing laparoscopic surgery and have shown adequate staging, less morbidity and better quality of life (10, 18-20). One limitation, however, is the difficulty in performing

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**TABLE 3: ANALYSIS OF DISEASE RECURRENCE AND OVERALL SURVIVAL FOR PATIENTS WITH ENDOMETRIOID HISTOLOGY**

<table>
<thead>
<tr>
<th>Recurrence Site</th>
<th>Vaginal apex</th>
<th>Pelvis</th>
<th>Retroperitoneum</th>
<th>Systemic</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IA</td>
<td>180</td>
<td>1.5</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>IB</td>
<td>54</td>
<td>2</td>
<td>11.8</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>II</td>
<td>12</td>
<td>2</td>
<td>11.8</td>
<td>1</td>
<td>5.9</td>
</tr>
<tr>
<td>IIIA</td>
<td>19</td>
<td>0</td>
<td>1</td>
<td>5.9</td>
<td>1</td>
</tr>
<tr>
<td>IIIB</td>
<td>18</td>
<td>0</td>
<td>2</td>
<td>5.9</td>
<td>1</td>
</tr>
<tr>
<td>IIIC</td>
<td>13</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>5.9</td>
</tr>
<tr>
<td>IV-IVA</td>
<td>6</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>IV-IVB</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

**TABLE 4: EFFECT OF BMI ON SHORT- AND LONG-TERM OUTCOMES**

<table>
<thead>
<tr>
<th></th>
<th></th>
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<td>1.39</td>
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<th>N (n=125)</th>
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<tbody>
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<td>N mean</td>
<td>N mean</td>
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<td>1</td>
<td>.1</td>
<td>1.3</td>
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<tr>
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<td>1</td>
<td>.1</td>
<td>1.6</td>
<td>.94</td>
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<tr>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No evidence of disease</td>
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<td></td>
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<td>Recurrence</td>
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<td>2</td>
<td>1.7</td>
<td>1</td>
<td>1.3</td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dead of other cause</td>
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<table>
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<tr>
<th>BMI CATEGORIES</th>
<th>-endometrioid</th>
<th>Serous</th>
<th>Clear cell</th>
<th>Carcinosarcoma</th>
<th>Sarcoma</th>
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<tr>
<td>(n=125)</td>
<td>Total number of patients</td>
<td>94</td>
<td>21</td>
<td>5</td>
<td>1</td>
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<tr>
<td>(n=15)</td>
<td>Number of recurrences</td>
<td>9</td>
<td>4</td>
<td>2</td>
<td>0</td>
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<tr>
<td>% recurrences</td>
<td>9.6</td>
<td>19</td>
<td>40</td>
<td>0</td>
<td>0</td>
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**TABLE 5: DISTRIBUTION OF RECURRENCES ACCORDING TO HISTOLOGIES FOR DIFFERENT BMI CATEGORIES**

<table>
<thead>
<tr>
<th>BMI&lt;30</th>
<th>Endometrioid</th>
<th>Serous</th>
<th>Clear cell</th>
<th>Carcinosarcoma</th>
<th>Sarcoma</th>
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<tbody>
<tr>
<td>(n=125)</td>
<td>Total number of patients</td>
<td>199</td>
<td>26</td>
<td>9</td>
<td>1</td>
</tr>
<tr>
<td>(n=17)</td>
<td>Number of recurrences</td>
<td>3</td>
<td>3</td>
<td>1</td>
<td>0</td>
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<tr>
<td>% recurrences</td>
<td>3.6</td>
<td>11.5</td>
<td>11.1</td>
<td>0</td>
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</tr>
</tbody>
</table>
these procedures in obese and morbidly obese patients, which comprise the majority of uterine cancer patients (4, 21). In the GOG LAP2 Study, conversion rates were 27% in women with BMI ≥35 kg/m² and 57% in women with BMI ≥40 kg/m² (18). Studies analyzing the outcomes of robotic surgery for uterine cancer have reported much lower conversion rates (10, 14, 21-24). This has also been our experience, and we believe that the robotic platform enhances the laparoscopic skills of the operator necessary when the patient has a challenging body habitus. The current study shows virtually no differences in the conversion rates for increasing BMI categories.

The GOG LAP2 Study, the largest randomized trial comparing laparoscopy and laparotomy for uterine cancer surgical staging, has shown that the risk of uterine cancer recurrence for laparoscopy versus laparotomy is small (19). Few studies have specifically addressed the impact of obesity on outcomes of uterine cancer patients (21, 22, 25). In a prospective cohort study, Calle, et al., found that risk of death from uterine cancer increases steadily with increasing BMI, with the most pronounced effect (6.25 times) for BMI >40 kg/m² (26). The present study finds opposite trends for the relationship between recurrence rates and obesity. Of 22 recurrences, 68.2% occurred in patients with BMI <30 kg/m². The differences in recurrent disease are pronounced when analyzed by BMI stratification: 15/125 patients (12%) for BMI <30, 7/239 patients (2.9%) for BMI = 30-39.9, 3/104 patients (2.9%) for BMI = 40-49.9, 1/28 patients (3.5%) for BMI >50. In this study, we found that the adverse effect of obesity on recurrence rates plateaus for BMI categories 30 and above.

Maintaining staging adequacy while minimizing surgical morbidity in obese patients with uterine malignancies is a longstanding conflict because of the specific anatomical challenges (21, 22). Lymphadenectomy was performed routinely in patients with a known diagnosis of uterine cancer, and the number of lymph nodes retrieved was adequate (27). One of the main concerns for robotic procedures is the longer operative times. We found no significant differences in operative times with increasing obesity. We have previously described that, at our institution, robotic operative times for uterine cancer staging were slightly shorter than for laparotomy (23). In the present study, the reported operative times are longer when compared to our previously reported results (23). This is explained by the fact that the trainees sitting at the console are allotted at least 30 minutes. Still, they compare favorably with the operative times published in previous studies (10, 21, 22, 28, 29). Short-term surgical outcomes, when analyzed separately for different BMI categories, have shown no clinically relevant differences [Table 4].

The recurrence-free survival of our patients compares favorably with the results reported by the largest study to date, the GOG LAP2 Study, where the three-year recurrence rate was 11.4% with laparoscopy and 10.2% with laparotomy (19). However, we found only one study investigating whether the robotic approach impacts the recurrence-free survival and overall survival for patients with uterine cancer (10). That study and the current study analyze a relatively large number of patients, and no adverse impact was found.

The weaknesses of our study include the retrospective design and the relatively short follow-up. The strengths are the large number of patients who underwent comprehensive surgical staging and the absence of patient selection.

The demographics and the results described here are also similar to previously published studies investigating long-term outcomes for uterine cancer patients. We hope that this study adds to the growing body of literature showing that obesity and super obesity are not barriers to achieving minimally invasive staging procedures for patients with uterine cancers.
REFERENCES:


OBJECTIVE

Recent studies have demonstrated decreased wound complications with closure of cesarean delivery skin incisions with subcuticular sutures. These studies have not adequately represented diabetic patients although these patients are at increased risk of complications. The objective of this study was to compare composite wound complication after suture and staple closure of cesarean delivery skin incision in diabetic patients. Our hypothesis was that subcuticular suture would be associated with lower risk of complication.

METHODS

Retrospective medical record review of 343 patients with gestational and pregestational diabetes who received prenatal care at resident or faculty clinics in two major tertiary care centers and underwent delivery by cesarean from January 1, 2009 to September 5, 2012. Subjects had Pfannenstiel skin incision with either staples or suture closure. Subjects were excluded if they did not have pre-pregnancy BMI information available. Our primary outcome was composite wound complication. Secondary outcomes were clinic visits, ED visits, readmissions and utilization of VNA services for wound care. Statistical analysis was performed using IBM SPSS software.

RESULTS

There were 343 subjects who met inclusion criteria. Of these, 201 had staple closure and 142 had suture closure. The staple and suture closure groups were similar in terms of age, gestational age at delivery, type of diabetes, duration of surgery and type of cesarean delivery. The patients who received staple closure were of higher pre-pregnancy BMI (mean 35.9 kg/m² compared with 31.3), higher gravidity (3.6 compared with 2.7), higher parity (1.4 compared with 0.9) and were more likely to smoke (14.4% compared with 2.1%). The patients who received staple closure were more likely to be cared for at Yale-New Haven Hospital (90.5% vs. 49.3%) and were more likely to be of Hispanic ethnicity (31.3% vs. 14.8%). Composite wound complication rate was lower with use of subcuticular sutures at 14.1% compared with 17.4% with staples; however, this difference did not reach statistical significance even after adjusting for confounders (p=0.41). When results were stratified by complication type, infection was found to be reduced to 4.2% with use of sutures compared with 8.0% in the staple group (p=0.55). There was also a trend toward reduced use of VNA services and reduced readmission for wound problems with use of subcuticular sutures, but these findings also did not meet statistical significance. Use of multivariate analysis with logistic regression did not reveal any statistically significant results.

CONCLUSION

Although results did not meet statistical significance, they do suggest that improved wound outcomes with the use of subcuticular sutures for closure of cesarean incisions are applicable to diabetic patients as well.
Evidence for Excessive Feto-Placental Activation of the Polyol Pathway: Implications For Hyperuricemia of Preeclampsia (PE)

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The Ohio State University Wexner Medical Center, Department of Obstetrics and Gynecology, Columbus, Ohio
Carl R. Darnall Army Medical Center, Department of Obstetrics and Gynecology, Fort Hood, Texas
The Research Institute at Nationwide Children’s Hospital, Center for Perinatal Research, Columbus, Ohio

OBJECTIVE

Hyperuricemia is a well-known finding in PE and has been associated with adverse outcomes, but its etiology has not been fully explained. Uric acid (UA) has been shown to be a byproduct of fructose (FRU) metabolism. Aside from ingestion, FRU is endogenously produced from glucose (GLU) via the polyol pathway: aldose reductase (ARD) converts GLU to sorbitol (SOR), and sorbitol dehydrogenase (SORD) converts SOR to FRU. ARD was originally isolated from the placenta. We hypothesized that overactivation of an existing polyol pathway in the feto-placental unit contributes to hyperuricemia of PE.

METHODS

FRU, SOR, GLU and UA were assayed in serum and urine specimens from 43 healthy pregnant women (CRLs) and 29 women with severe PE [sPE, gestational age (GA): 29±2w]. Cord blood (CB) serum of the sPE cases (n=23, delivery GA: 30±1) was assayed against matched CB from idiopathic preterm births (iPTB). CB from 22 term healthy mother/fetus dyads was also tested. mRNA expression of ARD and SORD was studied by real-time PCR and immunohistochemistry (IHC) in the placenta and amniochorion of sPE, iPTB and term pregnancies (n=4/group). Placenta and membrane explants were assessed for ability to produce SOR in culture after 24 hours.

RESULTS

In normal gestation, serum UA increased with GA (p<.001) in relationship with SOR (r=.67, p<.001) and FRU (r=.32, p=.03) but not GLU p>.05. Fractional excretion (FE) of FRU and UA decreased with GA (p<.001). sPE increased serum UA (p<.001) and SOR (p<0.001) but not FRU and GLU (p>0.05) vs. GA-matched CRLs. FE of UA, FRU and SOR but not of GLU were decreased in sPE (p<.001). In sPE, UA level was predicted by the combination of SOR and serum creatinine (p<.001 for both, together accounting for 53% of variability. SOR and UA in CB of healthy term newborns exceed maternal levels (p<.05 for both). sPE further increases CB SOR and UA vs. iPTB group (p<.05). PCR and IHC demonstrated preferential expression of ARD in trophoblasts and of SORD in decidual cells. Fetal membranes release threefold SOR compared to placenta in vitro.

CONCLUSION

An active polyol pathway is present in the feto-placental unit; overactivation of this pathway with accumulation of SOR in the context of decidual dysfunction may participate in increased UA in PE.
OBJECTIVES

An association between overactive bladder (OAB) and vaginal deliveries has already been established; however, the mechanisms involved are unknown. Human and animal studies have identified significant increases in Connexin 43 (Cx43), a key regulatory gap junction protein, in overactive detrusor muscles. The primary objectives of this study were to determine if vaginal distention (VD) alters smooth muscle and connective tissue gene expression and to determine if such changes are associated with increased gap junction gene expression in a murine model.

METHODS

Fifty-two female, nulliparous, C57BL/6 mice underwent VD via placement and filling of a transvaginal balloon catheter. Animals in which catheters were placed but not filled served as controls. Following treatment, mice were sacrificed at 1h (n=10), Day 2 (n=8), Day 3 (n=14), Day 4 (n=12), Day 7 (n=6), Day 20 (n=6) and Day 28 (n=6). The reproductive organs were removed en bloc, and the bladder was isolated for subsequent real-time PCR and Western blot analysis, using primers and antibodies to calponin, SM22 and Collagen 3A and Connexin 43; β-actin and β-tubulin and served as internal controls. Relative RNA and protein expression were compared using Student’s t-test. P<0.05 was considered statistically significant.

RESULTS

Calponin and SM22 mRNA expression decreased significantly in VD compared to controls with the highest decrease for both seen on Day 28 (an approximate six- and sevenfold decrease, respectively). There was no difference in COL3A mRNA expression between the two groups. A significant increase in calponin protein expression was noted initially, followed by a significant decrease. On Day 28, there was no difference in calponin protein expression between the two groups. SM22 protein expression was significantly increased on Days 7 and 28, and this was associated with a significant increase in Cx43 protein expression on Day 28.

CONCLUSION

Vaginal distention results in significant changes in bladder smooth muscle genes and upregulation of gap junction proteins. These responses may serve to restore bladder properties and function to the pre-distended states. Aberrant regulation of gap junction and/or smooth muscle proteins may result in altered intercellular communication, leading to OAB after VD.
OBJECTIVE

Transforming growth factor β (TGF-β3) controls the cellular proliferation in numerous cell types, including leiomyomas. Studies have shown that TGF-β3 is threefold to fivefold overexpressed in leiomyoma cells when compared to normal myometrial cells. We investigated the effects of peroxisome proliferators-activated receptor (PPAR) agonists on TGF-β3 expression. We examined the effects of PPAR agonists on leiomyoma cell growth.

METHODS

Human leiomyoma cells were isolated from surgical specimens. Women taking any hormonally active medications, such as GnRH agonists and oral contraceptive pills, were excluded. The cultured cells were treated with serum-free, phenol red-free media prior to treatment with increasing concentrations of PPAR agonists, rosiglitazone and troglitazone. After 24 hours of incubation, qRT PCR was utilized to determine TGF-β3 mRNA expression in treated cells compared to untreated cells. Data was analyzed using Student’s t-test.

RESULTS

TGF-β3 expression was significantly downregulated by treatment of leiomyoma cells with rosiglitazone. Cultured cells exposed to rosiglitazone had a sixfold decrease in TGF-β3 expression (p<0.05) compared to untreated cells. Utilizing concentrations of 1 and 10 uM rosiglitazone, no significant dose-responsive decrease in TGF-β3 was noted, with both concentrations demonstrating a similar decrease in TGF-β3 expression. After treatment with 10 uM of troglitazone, there was no significant change in TGF-β3 expression (0.79, p>0.05).

CONCLUSION

Our findings suggest that non-hormonal interventions aimed at downregulation of TGF-β3 offer a novel treatment option for leiomyomas. PPAR agonists, typically utilized to treat diabetes mellitus, offer the dual advantage of potentially inhibiting leiomyoma growth. With the appropriate patient selection and further studies, these findings offer potential new strategies for myoma treatment.
Morbidity of Appendectomy and Cholecystectomy in Pregnant and Non-Pregnant Women

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Yale Center for Analytical Sciences and Yale University School of Public Health, New Haven, Connecticut
Bayside Ob/Gyn, LLC, Providence, Rhode Island

OBJECTIVE

To use the data from the American College of Surgeons (ACS) National Surgical Quality Improvement Program to estimate major postoperative morbidity after 1) appendectomy in pregnant compared with non-pregnant women and 2) cholecystectomy in pregnant compared with non-pregnant women.

METHODS

We selected a cohort of reproductive-aged women undergoing appendectomy and cholecystectomy between 2005 and 2009 from the data files of the ACS National Surgical Quality Improvement Program. Outcomes in pregnant women were compared with those in non-pregnant women. The primary outcome was composite 30-day major postoperative complications. Pregnancy-specific complications were not assessed and thus not addressed.

RESULTS

Pregnant and non-pregnant women had similar composite 30-day major morbidity after appendectomy (3.9% [33 of 857] compared with 3.1% [593 of 19,172], p=.212) and cholecystectomy (1.8% [8 of 436] compared with 1.8% [584 of 32,479], p=.954). Pregnant women were more likely to have preoperative systemic infections before each procedure. In logistic regression analysis, pregnancy status was not predictive of increased postoperative morbidity for appendectomy (adjusted odds ratio 1.26, 95% confidence interval 0.87–1.82).

CONCLUSION

Pregnancy does not increase the occurrence of postoperative maternal morbidity related to appendectomy and cholecystectomy.
Obstetric Hemorrhage: Can an Easily Accessible Visual Aid Significantly Improve Provider Performance?

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Department of Obstetrics, Gynecology and Reproductive Sciences, Yale University School of Medicine, New Haven, Connecticut

OBJECTIVE

Postpartum hemorrhage complicates 1%-5% of deliveries in the United States and is a leading cause of maternal mortality worldwide. Visual estimation of blood loss is known to be inaccurate and imprecise. Obstetric hemorrhage requires expedient identification and intervention to prevent maternal morbidity and mortality. We aimed to create a visual aid (Figure 1) to improve accuracy of estimated obstetric blood loss and provider performance in obstetric hemorrhage situations.

METHODS

We designed a pocket card containing known volumes of blood on common obstetric materials and an algorithm for management of postpartum hemorrhage, which served as our visual aid. To assess accuracy of estimated blood loss before and after our intervention, we created six stations for estimation with known volumes of artificial blood, using materials common to standard delivery kits. Obstetric providers recorded visually estimated blood loss across a variety of volumes and materials before and after receiving our visual aid. We assessed the effects of actual blood volume, clinical role and years of experience on the accuracy of blood loss estimation. To compare pre- and post-intervention accuracy of estimated blood loss, we used the Wilcoxon Matched Pairs Signed Rank Test. We then had all available resident physicians from our obstetrics department respond to an unanticipated simulated postpartum hemorrhage, followed by administration of our pocket card and a subsequent postpartum hemorrhage simulation. Participant performance was scored for each simulation based on checklists for clinical response and knowledge of four common medications used in the management of postpartum hemorrhage (maximum score of 26).

RESULTS

A total of 151 participants assessed six stations for estimated blood loss. There was a significant improvement in accuracy of estimation of blood loss after visual aid administration across all blood volumes tested. Accuracy prior to intervention was significantly affected by provider type in two of the six stations (p=0.01 and p=0.03). This difference persisted in only one station after intervention (p<0.01). Years of experience did not correlate with accuracy of blood volume estimation in five of the six stations (p>0.05). Twenty-three obstetrics residents, including five new interns, six seasoned interns, six second-year, four third-year and two fourth-year residents, participated in the postpartum hemorrhage simulation. All residents demonstrated significant improvement in the management algorithm and medication knowledge after receiving the reference tool, with a pre-intervention mean score of 19.2 and a post-intervention mean score of 24.1 (p<0.0001). The new interns (n=5) participated in the simulation prior to starting clinical rotations and improved from a mean score of 14 to a mean score of 23 (p=0.02). One hundred percent of the residents considered operative intervention (either interventional radiology or laparotomy) within the five-minute simulation after receiving the reference tool, compared to 56% before intervention. On a post-simulation survey, 96% of participating residents reported that they felt “able to provide better patient care” with the reference tool.

CONCLUSION

Our novel reference tool improved obstetric provider accuracy of estimated blood loss, independent of provider type or years of experience.
experience, as well as resident physician performance in the management of simulated postpartum hemorrhage. Provision of such a visual aid to obstetric personnel could improve provider assessment of obstetric blood loss and may assist in expedient and appropriate management of hemorrhage situations.

Figure 1: Two-sided visual aid

Postpartum Hemorrhage - Management and Medications

<table>
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<th>Brand names</th>
<th>Dose</th>
<th>Contraindications</th>
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</thead>
<tbody>
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<td>Oxytocin</td>
<td>Pitocin</td>
<td>10-40 units in IL crystalloid IV</td>
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</tr>
<tr>
<td></td>
<td></td>
<td>10 units IM</td>
<td></td>
</tr>
<tr>
<td>Methylergonovine</td>
<td>Methergine</td>
<td>200mcg IM every 2-4 hrs; Maximum 3 doses</td>
<td>Hypertension; HIV on protease inhibitor or NNRTI</td>
</tr>
<tr>
<td>Carboprost tromethamine</td>
<td>Hemabate</td>
<td>250mcg IM every 20-90 minutes; Maximum 8 doses</td>
<td>Asthma/pulmonary disease</td>
</tr>
<tr>
<td>Misoprostol</td>
<td>Cytotec</td>
<td>1000 mcg PR</td>
<td>None</td>
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**INTRODUCTION**

Stress urinary incontinence (SUI), one of the most common forms of incontinence, has been consistently linked to vaginal delivery. Vaginal distention (VD) is a proposed mechanism of injury during delivery leading to SUI. VD consists of stretching and displacement of vaginal muscles and surrounding tissues, including the urethra. VD has been associated with decreased leak point pressure (LPP) in the mouse urethra.

**OBJECTIVES**

To evaluate alterations in urethral tissue protein expression in the mouse urethra after VD compared to non-distended controls over time.

**METHODS**

Sixty-six female C57BL/6 mice were ovariectomized and supplemented with estradiol for three days. Thirty-five mice had VD via transvaginal balloon catheter inflation while 31 mice received sham treatment. Mice were sacrificed at zero, two, three, four, seven, 20 and 28 days after VD. Protein lysates were prepared and used for Western blots (WB). Smooth muscle proteins (alpha actin, calponin, smoothelin and SM22) and connective tissue proteins (collagens 1 and 3 and tropoelastin) were analyzed with GAPDH as a loading control. WBs were analyzed by densitometry with Image J and compared in Excel using Student’s t-test; p<0.05 was statistically significant.

**RESULTS**

All smooth muscle proteins showed a transient decrease in expression either immediately after VD or at Day 2. Expression then increased as compared to the control group. These differences achieved significance in smoothelin on Day 2 and calponin and SM22 on Day 28. The connective tissue proteins collagen 1 and collagen 3 were both increased at all time points after VD compared to controls, achieving significance on Day 0 and Day 28. Tropoelastin was more variable, and no overall trend was observed.

**CONCLUSION**

Significant changes were observed in urethral smooth muscle and connective tissue proteins after VD. This suggests that urethral tissue remodeling occurs after VD to restore tissue properties and function to the pre-distended state. Aberrant or incomplete remodeling could contribute to decreased LPP and potentially to the development of SUI.
Cervical Carcinomas Overexpress Human Trophoblast Cell-Surface Marker (Trop-2) and Are Highly Sensitive to Immunotherapy with HRS7, a Humanized Monoclonal Anti-Trop-2 Antibody

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Division of Gynecologic Oncology, University of Brescia, Brescia, Italy

OBJECTIVE

We evaluated the expression of human trophoblast cell-surface marker (Trop-2) and the potential of hRS7, a humanized monoclonal anti-Trop-2 antibody, as a therapeutic strategy against treatment-refractory cervical cancer.

METHODS

Trop-2 expression was evaluated by real-time polymerase chain reaction (RT-PCR) and flow cytometry. Sensitivity to hRS7 antibody-dependent cell-mediated cytotoxicity (ADCC) and complement-dependent cytotoxicity was tested in five-hour chromium-release assays. The effect of interleukin-2 on hRS7 ADCC was also investigated.

RESULTS

High messenger RNA expression by RT-PCR and high Trop-2 surface expression by flow cytometry were detected in 80% of cervical cancers (four of five cell lines). Although these tumors were resistant to natural-killer cell-dependent cytotoxicity in vitro (mean killing 6.0%), Trop-2 positive cell lines showed high sensitivity to hRS7 ADCC (range of killing: 30.6%-73.2%). Incubation with interleukin-2 further increased the level of cytotoxicity against Trop-2 positive tumors.

CONCLUSION

hRS7 may represent a novel, potentially highly effective treatment option for patients with cervical cancer refractory to conventional treatment modalities.
INTRODUCTION

Endometrial receptivity is dependent on coordinated expression of signaling molecules, including BMP-2, HOXA10 and LIF. We have previously shown that TGF-β3, secreted by fibroids, alters the endometrial response to BMP-2. BMP-2 is a regulator of HOXA10 and LIF expression.

OBJECTIVES

To measure the concentration of TGF-β3 in fibroid-conditioned media (F-CM); to determine the effect of endometrial stromal cell (ESC) exposure to F-CM on expression of BMP receptors; to examine the effect of TGF-β blockade on BMP receptor expression in F-CM exposed ESC; to determine whether TGF-β blockade restores BMP-2 mediated HOXA10 and LIF expression in F-CM exposed ESC.

METHODS

Human ESC and fibroid cells were isolated from surgical specimens. ELISA was used to quantify TGF-β3 concentrations in conditioned media. Two approaches were used to block TGF-β. In the antibody-mediated approach, ESC was exposed to F-CM that was pre-incubated with TGF-β pan-specific antibody or control (non-specific IgG). In the transfection-mediated approach, ESC was transfected with a mutant TGF-β receptor type II (K227R mutation) expression vector or control (empty vector). Following transfection, cells were treated with F-CM or control (standard culture media). Subsets of cells were then exposed to recombinant human BMP-2 to assess BMP responsiveness after TGF-β blockade. qRT-PCR was used to determine expression of BMP receptor types 1A (BMPR1A), 1B (BMPR1B), 2 (BMPR2), HOXA10 and LIF. ELISA and PCR data were compared using Student’s t-test.

RESULTS

Mean TGF-β concentrations were more than fivefold greater in F-CM compared to conditioned media from ESC (52 ng/ml vs. 9.2 ng/ml, p<0.05). F-CM treatment of ESC reduced expression of BMPR1B and BMPR2 (0.61- and 0.59-fold, respectively, p<0.05). Pre-incubation of F-CM with TGF-β neutralizing antibody, prior to ESC treatment, prevented repression of BMP receptors. HOXA10 and LIF expression were repressed in ESC treated with rhBMP-2, subsequent to F-CM exposure (0.63- and 0.29-fold, respectively, p<0.05). Pre-treatment of F-CM with TGF-β antibody prevented HOXA10 and LIF repression. Similarly, HOXA10 and LIF expression were repressed in F-CM exposed ESC transfected with empty vector and treated with rhBMP-2 (0.33- and 0.64-fold, respectively, p<0.05). Transfection with K227R mutant TGF-β receptor prior to F-CM and rhBMP-2 exposure prevented repression of HOXA10 and LIF.

CONCLUSION

TGF-β, secreted by fibroids, impairs endometrial receptivity by altering BMP receptor expression and thus decreasing BMP-2 responsiveness. Blockade of TGF-β prevents repression of BMP-2 receptors and restores BMP-2 stimulated expression of HOXA10 and LIF.
OBJECTIVE

Gonadotropin releasing hormone agonists (GnRHa) are increasingly used for fertility preservation in women undergoing gonadotoxic chemotherapy. However, the mechanisms of action for these compounds have not yet been elucidated. In this study, we aimed to determine whether GnRHa has a direct effect on ovarian granulosa/cumulus cells.

DESIGN

Experimental study

METHODS

Gonadotropin releasing hormone receptor (GnRHR) expression was determined in mouse somatic and gonadal tissues, including granulosa/cumulus cells and oocytes using quantitative reverse-transcription polymerase chain reaction (qRT-PCR), Western blot analysis and immunohistochemistry. Granulosa cells were isolated from mouse ovaries primed with pregnant mare serum gonadotropin (PMSG). Response to GnRHa in cultured granulosa cells was assessed by determining: 1) cAMP response following transfection with a construct containing a luciferase reporter and a cAMP-response element and 2) phosphorylation of downstream mediators of GnRH signaling: ERK and p38. For all experiments, pituitary tissue and/or αT3-1 mouse pituitary cell line was used as a control.

RESULTS

GnRHR, mRNA and protein are expressed in mouse gonadal tissues as well as pituitary, heart and kidney, but were absent from lung and spleen. Within the ovary, GnRHR expression is high in granulosa/cumulus cells as well as oocytes. Following GnRH stimulation, we were unable to detect cAMP increase or activation of the ERK or p38 signaling pathway in cultured primary mouse granulosa cells, while activation was detected in the control αT3-1 mouse pituitary cells.

CONCLUSION

We have shown that gonadotropin releasing hormone receptor (GnRHR) is expressed in mouse granulosa/cumulus cells and oocytes. Activation of the canonical GnRH signaling pathways was not detected in our system. Our findings suggest that the mechanism of action of GnRHa in the ovary is either below the detection level of our experimental design or is different from that in the pituitary.
Amniochorion Apoptosis and Autophagy: Novel Insights into the Mechanisms of Iatrogenic PPROM after Fetoscopic Laser Surgery (FLS) for Twin Twin Transfusion Syndrome (TTTS)

R. Papanna, MD; L.K. Mann; K.J. Moise Jr.; T. Kyriakides; G. Zhao; P. Argoti; C.S. Buhimschi, MD; I.A. Buhimschi, MD
Department of Obstetrics, Gynecology and Reproductive Sciences, Yale University School of Medicine, New Haven, Connecticut

OBJECTIVE
Iatrogenic PPROM complication after FLS is interpreted as an iatrogenic mechanic event. We tested the hypothesis that, following FLS, fetal membranes become susceptible to PPROM through activation of apoptosis and autophagy pathways in the amniochorion cells.

METHODS
Extra-placental membranes from 31 pregnancies that underwent FLS for TTTS (GA procedure: 20±3w, GA birth: 30±4w, PPROM n=9) were prospectively collected at birth. Trocar insertion site (recipient sac), fetal membranes of the recipient and donor sacs, and the inter-twin membrane were evaluated for tissue morphology and connective tissue constituents using Masson’s trichrome and Movat’s staining. Collagen histochemistry was assessed with Sirius red and quantified by image analysis. Amniochorion sections were stained using various markers of proliferation (Ki67), mesenchymal and epithelial features (vimentin, cytokeratin), autophagy (beclin-1, LC3) and apoptosis (DNA fragmentation). CRL tissues came from monochorionic/diamniotic twin (idiopathic PTB, n=4) and healthy term singleton (elective CS, n=8) gestations.

RESULTS
Histological hallmarks of healing (angiogenesis, collagen deposition, granulation) or cellular proliferation (Ki67 staining) were absent at the trocar insertion site. Compared to CRLs, there was global loss of physiologic collagen organization in both amnion and chorion of the recipient and the inter-twin membrane, but not the donor sac (p<.001). The recipient amniochorion showed features of autophagy (beclin-1 and LC3 in clusters) and higher apoptotic index (highest at the trocar insertion site) compared to the donor sac (p=.03).

CONCLUSION
FLS for TTTS is associated with generalized alteration of structural integrity and amniochorion cellular damage of the recipient’s sac that likely contribute to PPROM.
Exploring the Epithelial to Mesenchymal Transition as a Mechanism of Placenta Accreta Formation

C. Duzyj, MD; C. Laky, MD; G. Zhao; M. Wehrum, DO; I. Buhimschi, MD; C. Buhimschi, MD  
Department of Obstetrics, Gynecology and Reproductive Sciences, Section of Maternal-Fetal Medicine, Yale University School of Medicine, New Haven, Connecticut

OBJECTIVE

The Epithelial to Mesenchymal Transition (EMT) is a cellular pathway involved in embryogenesis and early placental formation. This process is characterized by molecular and phenotypic alterations causing increased invasiveness and metastasis, the recapitulation of which has been implicated in wound healing and epithelial cancer progression. In cancer studies, loss of E-cadherin, a transmembrane protein involved in cell-cell adhesion, is a marker of EMT. Additionally, overexpression of the transforming growth factor-β (TGFβ), a known component of the uterine milieu, is implicated in the initiation of EMT. We interrogated the expression patterns of these key features of the EMT pathway in women with abnormally invasive placentation characteristic of placenta accreta.

METHODS

A cross-sectional study was conducted to determine the serum sE-cadherin and endoglin levels in non-pregnant women (n=15), healthy pregnant women (GA: 28 weeks; n=79 samples from 25 patients), women with placenta previa but no accreta (GA: 31 weeks; n=21) and patients with histologically confirmed invasive placentation (GA: 29 weeks; n=32 samples from 23 patients: accreta, n=5; increta, n=11; percreta, n=7), prior to blood transfusion or steroids. Expression level of sE-cadherin was assessed by Western blot and ELISA, and sEndoglin by ELISA. Myometrial-villous sections of hysterectomy specimens (n=15) were immunostained for cytokeratin-7 (epithelial marker), vimentin (mesenchymal marker), E-cadherin (C- and N-terminus domains), β-catenin (E-cadherin accessory protein), ADAM10 and presenilin-1 (E-cadherin cleavage proteins), endoglin (a ligand of the TGFβ system), TGFβ1, 2 and 3 and matrix metalloprotease 14 (MMP14, an endoglin cleavage protein). Normal placental bed biopsies (n=4), myometrium opposite from the site of placental insertion (n=4), myometrial biopsies from cesarean scars (n=9) and non-pregnant myometrium (n=4) served as controls.

RESULTS

1) In healthy CRLs, systemic sE-cadherin levels were higher in the first trimester than in non-pregnant controls or later GA (p=.029), while sEndoglin levels increased in the third trimester (p<0.001); 2) Women with advanced trophoblast invasion (increta and percreta) display circulating E-cadherin N-terminus immunoreactive cleavage bands, lower circulating levels of sE-cadherin (p=.006) independent of GA, and lower GA-corrected circulating soluble endoglin (p=0.005); 3) Extravillous trophoblasts (EVTs) of accretas but not controls immunostained for both cytokeratin and vimentin, consistent with EMT; 4) E-cadherin intracellular C-terminus immunoreactivity predominated over that of the extracellular N-terminus, consistent with preferential presenilin-1 processing; 5) Histological scoring showed that EVTs near the myometrial-villous junction had less E-cadherin expression compared to EVTs deeper in the myometrium (p=.001); 6) Increased intervillous space endoglin immunostaining was observed only in women with abnormal invasion (accreta vs. normal vs. previa p=.019); 7) Accreta EVTs showed a higher number of intra-cytoplasmic endoglin-positive granules compared to normal placental bed biopsies (p=.02); 8) Myometrial TGFβ1 staining was near-absent in the areas heavily populated by EVTs (p<.001) with no significant differences observed for TGFβ2 or 3; 9) MMP14 staining was higher in EVTs of samples with invasive placentation.
CONCLUSION

The Epithelial to Mesenchymal Transition appears to be active in women with accreta spectrum placental over-invasion. This knowledge may allow for development of novel diagnostic strategies by assessing levels of EMT signals in maternal serum, as well as development of new therapeutic and management strategies from cancer literature in women with known risk factors.
ABSTRACTS FROM RECENT SCIENTIFIC MEETINGS


ORAL PRESENTATIONS


Robotic Tumor Debulking in Stage IIC Fallopian Tube Carcinoma. G. Menderes, L. Clark, M. Azodi, D.A. Silasi.
Yale Oral Presentation at the American Urogynecologic Society 34th Annual Meeting, October 16-19, 2013, Las Vegas, Nevada

ORAL PRESENTATION

Unusual Presentation of Anterior Wall Vaginal Prolapse, Stump the Professors. A.M. McPencow, T.C. Chai.
ABSTRACTS FROM RECENT SCIENTIFIC MEETINGS

Yale Oral and Poster Presentations at the American Society for Reproductive Medicine 69th Annual Meeting, October 12-17, 2013, Boston, Massachusetts

ORAL PRESENTATIONS


The Role of miRNAs in Maternal to Zygotic Transition (MZT) of Mammalian Embryos. E. Babayev, O. Guzeloglu-Kayisli, E. Seli.

The Role of PUMILIO 1, a Translational Regulator, in the Mammalian Female Germline. W. Mak, D. Chen, K. Uyhazi, H. Lin.

POSTER PRESENTATIONS


H19 Expression Is Increased in Cumulus Cells of PCOS Patients Undergoing IVF. A.N. Kallen, C. Karakaya, E. Seli, Y. Huang.

H19 Expression Is Increased in Cumulus Cells of “High Responder” Women Undergoing IVF, as Compared to Normal and Low Responders. A.N. Kallen, C. Karakaya, E. Seli, Y. Huang.


ABSTRACTS FROM RECENT SCIENTIFIC MEETINGS

Yale Oral and Poster Presentations at the Society for Gynecologic Investigation 61st Annual Meeting, March 26-29, 2014, Florence, Italy

ORAL PRESENTATIONS


Insulin Regulates Glycogen Synthesis in Endometrial Epithelial Cells through a Novel Mechanism Unique to the Reproductive Tract. C. Flannery, G. Choe, F. Saleh, H. Taylor.

MiR-146a Regulates Antiphospholipid Antibody-Induced IL-8 Secretion by Human Trophoblast Cells. S.M. Gysler, L.W. Chamley, J.J. Brosens, V.M. Abrahams.


POSTER PRESENTATIONS


Endometriosis Located Proximal or Remote from the Uterus Differentially Alters Uterine Gene Expression: Distinct Systemic and Local Effects of Disease. H. Naqvi, G. Krikun, H.S. Taylor.


Differentiation of Endometrial Derived Stem Cells into Cardiomyocyte-Like Cells In Vitro. D. Hufnagel, L. Mutlu, H.S. Taylor.

Granulosa and Theca Cell Turnover in Mammalian Ovarian Follicles. J. Johnson, C. Wallace, C. Greene.


ABSTRACTS FROM RECENT SCIENTIFIC MEETINGS

Yale Oral and Poster Presentations at the Society for Maternal-Fetal Medicine 34th Annual Meeting, February 3-8, 2014, New Orleans, Louisiana

ORAL PRESENTATION


POSTER PRESENTATIONS


Focal Placenta Accreta Not Requiring Hysterectomy Has Alternate Risk Factors and Morbidity. C. Duzyj, C.S. Han, M. Mhatre, A. Cooper, M. Paidas, A. Sfakianaki.


THE YEAR IN REVIEW

WELCOME TO OUR NEW OB/GYN INTERNS

We are pleased to announce the interns for 2013-2014. All seven are outstanding and highly accomplished physicians.

PETER CHEN, MD, PhD
University of Wisconsin School of Medicine and Public Health

OLGA GRECHUKHINA, MD
Moscow Medical Academy (Preliminary)

LYDIA SHOOK, MD
Yale University School of Medicine

CHRISTOPHER DE HAYDU, MD
Mount Sinai School of Medicine

ABIGAIL CUTLER, MD
University of Chicago of the Biological Sciences
The Pritzker School of Medicine

ELISA JORGENSEN, MD
Yale University School of Medicine

ASHLEY PRITCHARD, MD
Columbia University College of Physicians and Surgeons

LYDIA SHOOK, MD
Yale University School of Medicine
OUR 2013 RESIDENCY PROGRAM GRADUATES AND THEIR NEXT DESTINATIONS

DARRAH CURIALE, MD
Private Practice
Boston, Massachusetts

LISA ZUCKERWISE, MD
Maternal-Fetal Medicine Fellowship
Yale University School of Medicine
New Haven, Connecticut

SAMI MAKAROUN, MD
Maternal-Fetal Medicine Fellowship
Magee-Women’s Hospital
Pittsburgh, Pennsylvania

ANTONIO MALDONADO, MD
Urogynecology Fellowship
University of Texas, Southwestern
Dallas, Texas

MARK SILVESTRI, MD
Robert Wood Johnson Fellowship
Yale University School of Medicine
New Haven, Connecticut

NATU MMBAGA, MD
Women and Infants
Health Care Alliance
Yale School of Medicine
Department of Obstetrics & Gynecology
Resident Staff 2013-2014

PGY-4
Asima Ahmad
Stephanie Bakaysa
Jonathan Black
Mai Hoang
Amanda Rostkowski
Janelle Warmington

PGY-3
Sudeshna Chatterjee
Stephen Collins
Catha Fischer
Gregory Gressel
Matthew Macer
Mohak Mhatre

PGY-2
Gary Altwerger
Kimberly Keefe
Devin Miller
Masaru Negi
Monica Pasternak
Lissa Yu

PGY-1
Peter Chen
Abigail Cutler
Christopher de Hayd
Olga Grechukhina
Elisa Jorgensen
Ashley Pritchard
Lydia Shook
Newest Additions to the Yale Faculty

**Sangini Sheth, MD**, has joined Yale as Assistant Professor in the General Gynecology section. Dr. Sheth obtained her medical degree from Johns Hopkins School of Medicine. She obtained her residency training in gynecology and obstetrics and a master’s of public health, both from Johns Hopkins.

![Sangini Sheth, MD](image)

**Vrunda Bhavasar Desai, MD**, has joined Yale as Assistant Professor in the General Gynecology section. Dr. Desai obtained her medical degree from the University of Medicine and Dentistry of New Jersey/Robert Wood Johnson Medical School. Her residency training in obstetrics and gynecology was obtained at New York Presbyterian Hospital-Weill Cornell. Her postdoctoral training in minimally invasive gynecologic surgery and da Vinci robotics training was received from North Shore University Hospital.

![Vrunda Bhavasar Desai, MD](image)
New Fellows On Board July 1, 2013

Gynecologic Oncology
Carlton Schwab, MD

Urogynecology & Reconstructive Pelvic Surgery
Jamie Chao, MD

Maternal-Fetal Medicine
Paul Hendrix, MD
Lea Tuzovic, MD
Lisa Zuckerwise, MD

Reproductive Endocrinology & Infertility
Cindy Duke, MD
Our 2013 Fellowship Graduates and Their Next Destinations

Leo Doherty, MD
Private Practice
IVF New Jersey
Somerset, New Jersey

Christina Duzyj, MD, MPH
Assistant Professor of Obstetrics and Gynecology
Robert Wood Johnson Medical School of Rutgers University
New Brunswick, New Jersey

Madeline Dick-Biascoechea, MD
University of Maryland, School of Medicine
Baltimore, Maryland

Saioa Torrealday, MD
Reproductive and Infertility Physician
Ft. Bragg Womack Army Medical Center
Fayetteville, North Carolina

Ramesha Papanna, MD, MPH
Assistant Professor
Division of Maternal-Fetal Medicine
The Texas Fetal Center, Dept. of Ob/Gyn
University of Texas Medical School
Houston, Texas

Joyce Varughese, MD
Clinical Assistant Professor of Ob/Gyn & Reproductive Medicine
State University of New York
Stony Brook, New York
PHOTO HIGHLIGHTS FROM THE APRIL 2013 ALUMNI REUNION IN NEW HAVEN, CONNECTICUT
PHOTO HIGHLIGHTS FROM THE 2013 C. LEE BUXTON RESIDENTS’ RESEARCH DAY
HONORING LEON SPEROFF, MD

Professor Emeritus of Obstetrics and Gynecology
Oregon Health & Science University
Portland, Oregon

When I am asked why I became an Ob/Gyn, why I stayed at Yale and why I am interested in reproductive endocrinology, I have a very easy answer: “My professors in medical school were Drs. Speroff, Glass and Kase. What choice did I have?”

The first edition of Clinical Gynecological Endocrinology and Infertility came out in 1973; six more editions followed, and it is now being published as Fritz and Speroff. And although Dr. Leon Speroff can be claimed by Case and Oregon, we all think of him as Yale, and have asked him to allow us to celebrate his career as the YOGS honoree of 2014.

Dr. Leon Speroff attended medical school at Case Western Reserve and came to Yale for his residency in obstetrics and gynecology. After serving in the Air Force for two years, he did a fellowship at the training program for steroid biochemistry at the Worcester Foundation for Experimental Biology in Shrewsbury, Massachusetts. He then worked with Dr. Raymond Van de Wiele at Columbia, before returning here to serve as the assistant chair to Dr. Kase and director of the gynecological endocrine laboratory.

Unfortunately, Dr. Speroff did migrate back to the lands west of the Hudson River, first to his alma mater, Case Western Reserve University, where he served as chair of reproductive biology, and then further west to Oregon Health & Science University, where his department honored him by establishing the Speroff Professorship to commemorate Leon’s “curiosity and creativity” in leadership in gynecologic research in reproductive endocrinology. Along the way, he has served as president of the American Fertility Society (now ASRM) and has held multiple posts in the North American Menopause Society.

There does not exist an aspect of reproductive endocrinology in the last 50 years that has not been researched and commented on by Dr. Leon Speroff. To celebrate and discuss these milestones, we are honored to have an all-star cast to visit with us. Dr. Nathan Kase, our esteemed chairman and co-author of THE book, will not only discuss their contributions to gynecological endocrinology, but will also give one of his famous lectures, guaranteed to make basic science thrilling and understandable. Dr. Burt Caldwell, Leon’s chief collaborator in the gynecological endocrine lab, will discuss some of the more entertaining aspects of lab life. Dr. John Hobbins will elaborate on clinical and research life in our Department in the 1970s and early 1980s, and has kindly agreed to emcee our dinner (and for those of you who remember the residents’ festivities in those days, John was some emcee!).

And we have a new addition to our festivities: the first YOGS film festival! Some of Dr. Speroff’s colleagues will, alas, be out of the country in early April, but have offered to send video tributes. So colleagues Drs. Marc Fritz, Phil DiSaia and Don Coustan will attend via video – and these are true stars as well.

Mary Jane Minkin, MD
Clinical Professor
Department of Obstetrics, Gynecology and Reproductive Sciences
Yale School of Medicine, New Haven, Connecticut
IN FOND MEMORY

Ingrid Liliana Cardenas, MD

Dr. Ingrid Cardenas passed away on February 20, 2013.

Dr. Cardenas was born and raised in Bogota, Colombia. She attended medical school at the National University of Colombia and completed residency in Ob/Gyn. Ingrid then went on to a clinical fellowship specializing in high-risk pregnancies and reproductive endocrinology. In 2007, Ingrid came to Yale for a research fellowship with Dr. Gil Mor. She collaborated with many members of the Department and authored several manuscripts in the four years she was at Yale. She also met her husband Paul and gave birth to their son Charlie while living in New Haven. In 2011, Ingrid was accepted to the Ob/Gyn residency program at Tufts University Medical Center in Boston. During her second year of residency, Ingrid was diagnosed with gastric cancer. She underwent extensive surgery and chemotherapy, all the while continuing her residency and tending to her family.

Ingrid was a kind-hearted and loving woman. Her passion and vibrant personality touched the hearts of many. She was a respected colleague and dear friend.

Joel Silidker, MD

Dr. Joel Silidker passed away on July 6, 2013.
(This eulogy was written by a dear friend, Dr. Susan Richman)

The long and the short of it: I would not have survived the four-year, 100+-hours-a-week trial by fire without his help and support. He made life better the first day I met him, July 1, 1979. Fresh out of medical school and scared out of our wits, the five out of six of us, destined to travel through the war zone as a group, met at our one-day orientation. The sixth intern just did not show up; when Joel finally reached her, after several desperate phone calls, she admitted to having accepted two positions and decided to take the one in Florida instead of the one at Yale! Thus we started our training under a black cloud. No worries, said Joel, we can handle it. He could do the work of two – or three if he had to. And he often did.

Our first formal rotation together was as junior residents, assigned to Waterbury Hospital; the two of us and a senior resident, supposedly supervising us. The first morning we arrived alone at 5 a.m. to begin rounds on 20 or 30 patients, knowing very little about the patients, the system or what we were looking for. We clung to each other like barnacles, supplementing each other’s skills and knowledge to the best of our limited ability. When we got called to the delivery floor, total panic set in; we had no experience, as our internship year had been divided between medicine/surgery and pediatrics! But by the good graces of the nurses, we managed to pull off a normal delivery. We were bonded for life after that.
When I got pregnant at the end of senior year, he (and Bobby) stayed happy and supportive throughout the experience, allowing me to bank my vacation time ahead and take my full two weeks off afterwards. A far cry from the six weeks of leave or 12 weeks FMLA that are standard nowadays, but Joel got me through that as well. The baby blues that followed did not stand a chance with Joel around to tell jokes and put life into perspective for me. He could ALWAYS do that with aplomb.

His was a beautiful face, one that exuded kindness, caring and support. He always told me that we would get through anything together, never fear. He meant it and lived it every day. He was everything one could hope for in a co-worker: strong, decisive, honest, hardworking, reliable, efficient, smart and skilled. And he knew how to live, not just exist. His top two rules were:

**Work Hard, Play Hard**

He indoctrinated every resident applicant and incoming intern with his zest for life; he could list 50 things he loved about his career and about living in the Greater New Haven area. He exuded joy as he spoke. He invited as many trainees as possible to his home for dinner or holidays, so that none were ever “homeless.” He loved to eat, and made sure that everyone stuck in the hospital ate well. Dinner in the cafeteria was never the meal of choice for him; it had to be take-out Chinese, or pizza, or Greek Olive fare. He proved that sometimes you can even play WHILE you are working! And he could play with his food for a laugh: dancing lobsters or chickens, for example. He would have made as good a *Saturday Night Live* host as any.

**You Can Get Old Once, But You Can Be Immature Forever**

He provided comic relief from the stress of hospital life: he dressed in a gown and hung red and green ornaments from his ears every Christmas; dressed as a corpse every Halloween. He was always the life of the party; long nights on call were also a party if he was around.

I am forever grateful for having had him in my life, for the good times and the bad. He is irreplaceable. I am hoping the memories can sustain me in his absence. I will always be expecting him to call me by 7 a.m. each morning, as he had for the past 34 years, and ask me:

“\What’s new, where are you working and when are you done?\”

“\When can we get together?\”

And most of all: “Is your life in balance?” If it was not, “What can I do to help?” – because he could fix anything I could throw at him.
BIRTH ANNOUNCEMENTS

Congratulations to the Yale Ob/Gyn doctors who recently welcomed new babies:

**Arya Noor Khan** – 6 pounds, 14 ounces
May 3, 2013 (Asima Ahmad, MD and Ali Khan)

**Kaden Kenneth Lau** – 6 pounds, 8 ounces
May 19, 2013 (Christina Han, MD and Rodman Lau)

**Navid Ghazal Barth** – 7 pounds
October 17, 2013 (Sanaz Ghazal, MD and Sandon Barth)

**Rohan Desai** – 7 pounds, 8 ounces
December 1, 2013 (Vrunda Desai, MD and Nihar Desai, MD)
GRANTS AWARDED

Hugh Taylor, MD – OvaScience – Endometriosis Biomarker and Novel Therapy Discovery Research

Sabrina Diano, PhD – NIH/NIDDK, R01DK097566 – “Role of Peroxisome Proliferation in Leptin Resistance”

Aileen Gariepy, MD, MPH – NIH YCCI Scholar – “What is the relationship between pregnancy intention and preterm birth?”

Joshua Johnson, PhD – NIH/NICHD, R21HD071873 – “Use of a Fragile X premutation knock-in mouse to study FXPOI”

Amanda Kallen, MD – NIH RSDP Scholar – “H19 I ncRNA-mediated regulation of gene expression in granulosa cells”

Katie Lowther, PhD – Lalor Foundation Lalor Fellow – “Regulation of maternal mRNA translation during oogenesis by embryonic poly(A)-binding protein (ePAB)”

Elena Ratner, MD – Ovarian Cancer Research Fund – Woman to Woman Program

Yang Yang, PhD – Ovarian Cancer Research Fund – “P53 aggregation: a new target to combat ovarian cancer platinum-resistance”

Gil Mor, MD, PhD – NIH Services in Support of the Perinatology Research Branch

Gil Mor, MD, PhD – CanTx/Novogen – “Targeting Ovarian Cancer Stem Cells”

Emre Seli, MD – NIH/Thomas Jefferson University – “The Anti-inflammatory mRNA-Binding Protein ZFP36 in Obesity and Metabolism”

2013 McKern Award Recipients:

Winifred Mak, MD, PhD

Ayesha Alvero, MD

Michelle Silasi, MD

Women’s Reproductive Health Research Program K12

Dr. Michelle Silasi has been appointed the newest WRHR scholar, joining continuing WRHR scholars Drs. Elena Ratner and Winifred Mak.
PRESS GANEY PATIENT SATISFACTION SURVEY

In the most recent Patient Satisfaction Survey from Press Ganey, the national leader in patient satisfaction measurement, our practices received the following scores in Overall Practice Assessment:

- Yale Gynecologic Oncology (91.3)
- Yale Maternal-Fetal Medicine (88.7)
- Yale Reproductive Endocrinology (91.7)
- Yale Urogynecology (91.0)

YALE OB/GYN PHYSICIANS ON 2013 TOP DOCS LISTS

In New York Magazine’s annual “Best Doctors” issue, four physicians from Yale’s Department of Obstetrics, Gynecology and Reproductive Sciences were recognized:

Masoud Azodi, MD (Gyn Oncology)
Joshua A. Copel, MD (MFM)
Michael J. Paidas, MD (MFM)
Pasquale Patrizio, MD, MBE (REI)

Closer to home, Connecticut Magazine recognized six as “Top Doctors” in their 2013 annual survey:

Ian M. Cohen, MD (Associated Women’s Health Specialists PC)
Ljiljana Plisic, MD (County Ob/Gyn Group PC)
Emily E. Blair, DO (Ob/Gyn of Fairfield County)
Mary Jane Minkin, MD (Obstetrics, Gynecology & Menopause Physicians)
Peter E. Schwartz, MD (Yale Department of Obstetrics, Gynecology and Reproductive Sciences, Gyn Oncology)
Musa L. Speranza, MD (Obstetrics, Gynecology & Menopause Physicians)
U.S. NEWS & WORLD REPORT NAMES YNHH ONE OF THE NATION’S TOP HOSPITALS

Yale University/Women’s Health Programs Ranked #9 in Women’s Health by U.S. News & World Report

YNHH Ranked #14 Nationally in Gynecology by U.S. News & World Report

U.S. News & World Report’s “Top Doctors” annual issue included 20 of our Ob/Gyn doctors:

Masoud Azodi, MD (Yale Department of Obstetrics, Gynecology and Reproductive Sciences, Gyn Oncology/YNHH)

Emily Blair, DO (Bridgeport Hospital)

Karol Chacho, MD (Bridgeport Hospital)

Joshua Copel, MD (Yale Department of Obstetrics, Gynecology and Reproductive Sciences, MFM/YNHH)

Julia Cron, MD (Obstetrics, Gynecology & Menopause Physicians Group/YNHH)

Joseph Cuteri, MD (Bridgeport Hospital)

Robert Deal, MD (Bridgeport Hospital)

Emily Fine, MD (Gynecology Group/YNHH)

Marsha Guess, MSc, MD (Yale Department of Obstetrics, Gynecology and Reproductive Sciences, Gyn Urology/YNHH)

Steven Laifer, MD (Bridgeport/Greenwich Hospitals)

Vincent Lynch, MD (Greater New Haven Ob/Gyn Group PC/YNHH)

Urania Magriples, MD (Yale Department of Obstetrics, Gynecology and Reproductive Sciences, MFM/YNHH)

Michael Paidas, MD (Yale Department of Obstetrics, Gynecology and Reproductive Sciences, MFM/YNHH)

Pasquale Patrizio, MD, MBE (Yale Department of Obstetrics, Gynecology and Reproductive Sciences, REI/YNHH)

Thomas Rutherford, MD, PhD (Yale Department of Obstetrics, Gynecology and Reproductive Sciences, Gyn Oncology/YNHH)

Alessandro Santin, MD (Yale Department of Obstetrics, Gynecology and Reproductive Sciences, Gyn Oncology/YNHH)
Peter Schwartz, MD (Yale Department of Obstetrics, Gynecology and Reproductive Sciences, Gyn Oncology/YNHH)

Dan-Arin Silasi, MD (Yale Department of Obstetrics, Gynecology and Reproductive Sciences, Gyn Oncology/YNHH)

Robert Stiller, MD (Bridgeport/Greenwich Hospitals)

Hugh Taylor, MD (Yale Department of Obstetrics, Gynecology and Reproductive Sciences, REI/YNHH)

RECORD NUMBER OF ALUMNI IN PRESTIGIOUS POSITIONS

It is a testament to our program excellence that so many of our faculty, fellows and residents have gone on to secure highly regarded positions in the American medical field. These include:

- 26 Chairs of Obstetrics and Gynecology
- 5 Deans of Medical Schools
- 5 Key Positions at the National Institutes of Health
- 7 Institute of Medicine Members

WHERE IN THE WORLD …

Please take a look at the list below and help us locate some of our more elusive alumni!

Stuart Adams, MD
Michael Kelly, MD
Orlando J. Miller, MD
Alison Shearer-Deep, MD

If you know their whereabouts, please let them know that we are trying to contact them to include them in our Society. Contact info may be mailed to yogs@yale.edu.

DID YOU KNOW?

Hugh S. Taylor, MD, department chair and the Anita O’Keeffe Young Professor of Obstetrics, Gynecology and Reproductive Services, has been awarded the International Fundación IVI Award for best clinical research record in reproduction medicine. Dr. Taylor was chosen for this prestigious honor for having published the papers with the highest impact in this field over the past five years. Additionally, Dr. Taylor was elected President of the Society for Gynecologic Investigation (SGI).

Jessica Illuzzi, MD, is leading the Laborist Division at the Chapel Street Campus. She established a collaborative practice with the midwives formerly based at St. Raphael’s, as well as with the Yale School of Nursing Midwife Practice.
Nancy Stanwood, MD, MPH, FACOG, FSFP, is Chair of the Board of Physicians for Reproductive Health, a national advocacy organization dedicated to bringing the voice of practicing physicians and the best medical evidence in reproductive health to the policy arena.

Linda Fan, MD, FACOG, is the Director of the new Gynecology Division. Dr. Fan’s team oversees the care of the Gynecology Service at the Women’s Center and Chapel Street Campus.

Linda Fan, MD, FACOG, and David Lima, MD, are heading a new quality assurance initiative in Gynecology, which started in November 2013; they began interviewing for eight residency positions to be filled in July 2014. With this increased residency complement, we will be able to fully staff the Chapel Street Campus and expand educational opportunities for the residents.

Toby Chai, MD; Richard Bercik, MD; Marsha Guess, MSc, MD, and Leslie Rickey, MPH, MD, are leading the Female Pelvic Medicine and Reconstructive Surgery Program. This group unites a team of gynecologists and urologists into a single practice that brings an enhanced level of care for female pelvic floor disorders.

Joshua Copel, MD, was appointed to the Division of Maternal-Fetal Medicine of the American Board of Obstetrics and Gynecology.

Vikki M. Abrahams, PhD, was awarded the 2013 American Society for Reproductive Immunology’s J. Christian Herr Award for Excellence in Reproductive Immunology Research.

Aileen Gariepy, MD, MPH, FACOG, was nominated by our resident, Dr. Greg Gressel, for the American Congress of Obstetricians and Gynecologists District 1 Mentor of the Year and was awarded this important recognition of her teaching excellence. Dr. Gressel acknowledged the crucial support Dr. Gariepy provided in his research project, including mentorship for grant funding from ACOG, project design and conduct, and a successful submission to the ACOG Annual Clinical Meeting in May 2013, for which Dr. Gressel did an oral presentation.

Michael Paidas, MD, was elected to the Medical and Scientific Advisory Council (MASAC) of the National Hemophilia Foundation, a three-year appointment. Dr. Paidas is also a member of the Society for Maternal-Fetal Medicine and the American College of Obstetricians and Gynecologists Working Group for Deep Venous Thrombosis Prevention Patient Safety Bundle. The recommendations of the group were presented at ACOG, CDC, SMFM Maternal Mortality Study Group and Consensus Meeting during the 61st Annual Clinical Meeting of ACOG, and were supported by the Federal Maternal and Child Health Bureau. Dr. Paidas was one of two recipients of the Dean’s Award of the Tufts Medical Alumni Association, presented at the Kennedy Library, Boston, Massachusetts. He received an Honorary Degree, Master of Arts, from Yale University.

Alessandro Santin, MD, was a senior author on a paper published in February 2013 in Proceedings of the National Academy of Sciences (PNAS) entitled “Landscape of Somatic Single-Nucleotide and Copy-Number Mutations in Uterine Serous Carcinoma.” He worked in collaboration with the Department of Genetics, Howard Hughes Medical Institute, Pathology, Pharmacology and Institute of Molecular Medicine, Brescia, Italy. In a major breakthrough for uterine serous carcinoma (USC), a chemo-resistant, aggressive form of endometrial cancer, Yale researchers have defined the genetic landscape of USC tumors, findings that point to new treatment opportunities. Dr. Santin was quoted: “We have clearly identified the mutations that are responsible for USC tumors. . . . In addition to a number of well-known cancer genes, we found three genes that had not previously been associated with cancer that
are found in these tumors. This finding points to new pathways that could be important in developing therapies down the road.”

Nita Maihle, PhD, has accepted a position as Associate Director for Education at the Georgia Regents University Cancer Center, Augusta, Georgia.

Jonathan Black, MD, and Amanda Rostkowski, MD, have been elected the Administrative Chief Residents for the academic year 2013-2014.

Mohak Mhatre, MD, PGY-3, is one of five recipients of the Edward Quilligan Scholarship of the SMFM. This new program was initiated by the SMFM to “identify individuals in their PGY-3 year of obstetrics and gynecology residency education who exhibit leadership, commitment and interest in teaching, research or public policy.” Dr. Mhatre was selected from over 50 candidates from top residency programs around the country.

Yale Obstetrics, Gynecology and Reproductive Sciences and the Yale School of Management offer a 24-month fellowship to a post-resident who aspires to an administrative position in private or academic practice.

Fundraising: Discovery to Cure has received over $200,000 this year; over $150,000 was raised from the Sixth Annual Discovery to Cure Walk to benefit ovarian cancer research, which was held at Sherwood Island State Park in Westport, Connecticut, on September 15, 2013.

The Maternal-Fetal Medicine Preemie-Donnas annual fundraiser in support of the March of Dimes for Babies received over $1,200 this year.

FACULTY PROMOTIONS EFFECTIVE JULY 1, 2013

Heather Lipkind, MD, to rank of Associate Professor
Christian Pettker, MD, to rank of Associate Professor
Emre Seli, MD, to rank of Professor

VOLUNTARY FACULTY PROMOTIONS EFFECTIVE JULY 1, 2013

Howard Shaw, MD, to rank of Clinical Professor
Robert Stiller, MD, to rank of Clinical Professor
JOEL SILIDKER, MD MEMORIAL FUND

We are pleased to announce the creation of the Dr. Joel Silidker Memorial Fund. With this initiative we will pay tribute to a remarkable man, compassionate physician and generous friend.

Our aim is to raise enough money to endow an annual department lecture, the Joel Silidker Memorial Lecture, focusing on Humanism in Medicine.

We also hope to raise enough to create a second-year resident award that would be presented to the resident who embodies the humanistic qualities and love of life that defined Joel.

In order to endow such a fund, we need to raise a minimum of $100,000. The income from this endowment will allow the lecture in Joel’s name to be a permanent part of the Department. Each year we will remember and pay tribute to Joel. This will serve to remind everyone of Joel’s character and actions; hopefully, it will also inspire us all as he did in life.

In order to move this project forward, Leonard Silidker, Joel’s father, has promised to match the funds we raise dollar for dollar (up to $50,000). This is a great opportunity, and we don’t want to leave any money on the table. Please consider a generous contribution, and thank you in advance for your partnership.

Contributions can be sent to:

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Joy.carrigan@yale.edu
PETER E. SCHWARTZ, MD PROFESSORSHIP FUND
OBSTETRICS, GYNECOLOGY AND REPRODUCTIVE SCIENCES

We are proud to announce the establishment of the Peter E. Schwartz, MD Professorship Fund in honor of Dr. Peter Edward Schwartz, mentor, distinguished colleague, caring doctor and great friend. Early in his journey, Peter demonstrated care and concern for women’s personal health issues, and is credited with developing novel means of diagnosing and treating ovarian cancer and establishing the current standard of care for the treatment of women with serous carcinoma of the uterus. The professorship’s purpose will be to support the work of someone following the path of Dr. Schwartz, focusing on basic and clinical research involved with reproductive cancers and programs in women’s health.

The highest honor a university can bestow upon a faculty member is an endowed professorship. At Yale School of Medicine, an endowed professorship distinguishes its namesake and holder as a leader in medicine. The endowed professorship also ensures that the particular focus and restrictions of the Chair are advanced in perpetuity, transcending the tenure of any individual faculty member.

Dr. Schwartz has cared for women with gynecological malignancies at Yale for over 40 years, and has a continued research interest into biomarkers for the earlier detection of ovarian cancer. His achievements were acknowledged in 2006 when then Governor Jodi Rell proclaimed November 18th as Dr. Peter Schwartz Day in Connecticut. In November 2012, he was honored with the Yale Cancer Center Lifetime Achievement Award and recognized as a pioneer and innovator in the field of gynecologic oncology. His clinical research focus is on the use of neoadjuvant therapy for ovarian cancer and aggressive uterine cancer. He has never pontificated about his contributions, and few know all his accomplishments. However, it is widely known that many of his early theories, treatments and procedures are now recognized as the gold standard to be followed when treating all forms of reproductive cancers. Dr. Schwartz has consistently advocated for a multidisciplinary approach to cancer care and treatment, calling on his colleagues from radiology, pharmacology, medical oncology, surgery, the School of Nursing, etc., and has made education a priority throughout his tenure at Yale School of Medicine.

Please consider making a generous contribution in honor of Dr. Schwartz.

For Giving Information – please contact

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Office of Development
P.O. Box 7611
New Haven, CT 06519
203-436-8541
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BLOGS

Yale Fertility Center Blog: http://yalefertilitycenter.blogspot.com/

Yale Reproductive Endocrinology Blog: http://yalereproductiveendocrinology.blogspot.com/

FACEBOOK PAGES

Yale RE: http://www.facebook.com/pages/Yale-Reproductive-Endocrinology/68087952760

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WE WANT TO SHARE YOUR SUCCESSES!

Everyone’s favorite part of an alumni magazine is the section listing professional and personal updates, and YOGS alumni are no exception! But to keep this part of the YOGS Journal current, we need your help. If there is any news you’d like to share with your Yale family – about your career, personal achievements, family or anything you think your friends would like to know – please update us by filling out and returning the form below.

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Attn: YOGS Coordinator

All submissions must be made in writing. Class notes may be edited for clarity and space. Due to limited space, the YOGS Journal cannot guarantee the publication of all items.
As a member or future member of YOGS, you may already be well aware of the many benefits membership brings – inclusion in society events, the latest Ob/Gyn news and information, invitations to lectures and workshops, and of course the annual YOGS Journal.

But to keep our Society functioning at the highest level, we need your continued support. If you’ve already paid your annual dues, thank you! If you haven’t, please take a moment to fill out the form below and return it to us with payment as soon as possible. And please consider becoming a lifetime YOGS member so you’ll never miss any of the benefits of membership.

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