We are very pleased to announce that Hugh S. Taylor, MD, has been named Chair of the Department of Obstetrics, Gynecology and Reproductive Sciences at Yale School of Medicine and Chief of Obstetrics and Gynecology at Yale-New Haven Hospital, effective October 1, 2012.

Dr. Taylor is well known to the Yale medical community, having served as professor and vice-chair of obstetrics, gynecology and reproductive sciences and as Chief of Reproductive Endocrinology and Infertility. A graduate of Yale College and the University of Connecticut School of Medicine, he completed his residency at YNHH in 1992, followed by a postdoctoral fellowship in molecular biophysics and biochemistry at Yale and a fellowship in reproductive endocrinology and infertility.

Dr. Hugh Taylor brings an outstanding record of accomplishment as a clinician, educator and researcher. His research has been continuously funded by the NIH for more than 20 years. He is the editor-in-chief of the journal Reproductive Sciences and editor of Endocrinology. He serves on the board of directors of the American Society for Reproductive Medicine (ASRM), where he is president-elect of the endometriosis interest group and on the governing council of the Society for Gynecologic Investigation (SGI). Dr. Taylor received the prestigious President’s Achievement Award from SGI in 2008.

Dr. Taylor is an active clinician who is highly regarded by practicing physicians in the community and by physicians on the full-time faculty. As Chief of Reproductive Endocrinology and Infertility, Dr. Taylor has successfully grown the clinical capability and geographic reach of this critical service. Under his leadership, the section has established itself as a national leader, reflected in Dr. Taylor’s role as Clinical Director of the Society for Assisted Reproductive Technology, the organization that governs in vitro fertilization practice in the United States. Dr. Taylor has been recognized as Mentor of the Year by the American College of Obstetricians and Gynecologists and as Honoree of the Year by the Endometriosis Foundation of America. He has received multiple research awards from ASRM and the Endocrine Society. We would like to express our deep gratitude to Peter E. Schwartz, MD, who led the department with his characteristic dedication and level of excellence as interim chair since last August.

Robert J. Alpern, MD
Dean and Ensign Professor of Medicine
Yale School of Medicine

Marna P. Borgstrom
CEO, Yale-New Haven Hospital
President & CEO, Yale-New Haven Health System

Note: Since publication of this announcement, Dr. Taylor has been awarded the International Fundación IVI Award for best clinical research record in Reproductive Medicine. Additionally, Dr. Taylor was elected President of the Society for Gynecologic Investigation (SGI).
Contributors

Editor-In-Chief – Mary Jane Minkin, MD

Managing Editor – Dianna Malvey

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EDITOR’S NOTE

The great humorist Garrison Keillor always begins his monologues, “It’s been a quiet week in Lake Wobegon, my hometown.” This past year has not been a quiet year in New Haven. We’ve had some significant and terrific changes. All of you know that our very own Dr. Hugh Taylor – our first chair raised at Yale (born, residency, fellowship, faculty!) – was appointed on October 1, 2012. As always, Dr. Peter Schwartz had done a wonderful job of running the Department in the interim after Dr. Charles Lockwood moved west of the Hudson River.

We also had a major change in the administration for our outstanding clinical faculty of community physicians. Dr. Larry Wartel resigned as associate chief of the Department after over 24 years of service. Dr. Steve Fleischman was chosen by the community to lead us. In this role, Steve continues to show his enormous talent to be everywhere at once. His energy persists – being fully active in organizing the private community, working in his practice, teaching and continuing to work in ACOG and local medical societies.

Hugh immediately had to appoint a new section head for Reproductive Endocrinology, and he appointed another of our longtime favorites, Dr. Emre Seli, to run the section. Emre has extensive clinical and research activities in both the infertility and endocrinology aspects of the section.

And as our official title is not only Obstetrics and Gynecology, but also Reproductive Sciences, Hugh appointed Dr. Gil Mor to serve as the chief of the new official section of Reproductive Sciences. Gil, the only human who can truly make apoptosis exciting, will continue to help our Department translate our extensive basic science research to valuable clinical applications.

And stay tuned: we are in the midst of a national search to appoint a permanent section chief of both Urogynecology (alas, Dr. Kathy Connell also left us to go west of the Hudson River to Colorado) and Maternal-Fetal Medicine.

Our residency and fellowship programs continue to thrive; Hugh has asked Dr. Lubna Pal to officially be in charge of educational activities for our trainees. As you will see from our journal, our trainees continue to do and present wonderful projects and land excellent positions to continue their work.

And to celebrate our Department (remember, we still maintain that everyone who is anybody in Ob/Gyn in this country has at most one degree of separation from Yale), we are commemorating the career of Dr. Roberto Romero as our YOGS honoree this year. We have assembled a truly amazing group of experts to come back to Yale to celebrate their careers here as well as Roberto’s career. We are hoping that everyone will have a fabulous time socializing and learning.

I hope I will get to see many of you in New Haven this April – but if you cannot make it, I hope that reading this journal will update you on life here.

Mary Jane Minkin, MD, FACOG
It is a great honor to introduce myself as the new Associate Chief of Obstetrics and Gynecology at Yale-New Haven Hospital. I want to thank Dr. Wartel for all his years of service representing the community and his dedication to the Department.

What an exciting first year and a half it has been since assuming this role! At our first meeting after I was appointed to this role, Dr. Lockwood announced that he was leaving. Since then we have been through an extensive national search for a new chair, culminating in the exciting appointment of our very own Dr. Hugh Taylor. I know I speak on behalf of the entire YOGS community in congratulating him on this wonderful accomplishment. I am sure he will continue to build upon the outstanding tradition and history of our Department.

A historic event in 2012 was the acquisition of the Hospital of St. Raphael by Yale-New Haven Hospital. With the addition of the St. Raphael’s Campus (SRC), our Department truly has an opportunity to look at healthcare delivery across an entire community. Our Department is clearly on the forefront of this transition as the medical staff in Ob/Gyn at SRC have always been active participants in the educational mission. Coordinating the services across the campuses is now under way, and we will be planning for the future as one unified Department.

On February 1, 2013, the entire Yale-New Haven Hospital went live with EPIC for inpatient and outpatient services, and June 1 will see the SRC come online as well. In addition, the majority of community practices have committed to transitioning to EPIC in the coming year. As we witness the evolution of the Affordable Care Act, we hope the unification of patient records across the institution will allow the entire Department to work collaboratively on improving the delivery of service in women’s healthcare.

In another step toward improving the model for delivery of services to women in the greater New Haven area, the 2012/2013 academic year also saw the development of a stronger relationship between the community physicians at YNHH and the Yale Medical Group/Yale University School of Medicine. Four community practices have signed affiliation agreements with the Yale Medical Group, bringing an opportunity for improving healthcare delivery in New Haven and across Connecticut. Our Department has always had a rich heritage of working together on educating residents and medical students, patient safety and quality improvement programs, and these affiliations will continue to strengthen these endeavors.

Our voluntary faculty continues to be heavily involved in fulfilling the mission of the Department. Under the leadership of Dr. Taylor, we are looking forward to keeping you abreast of the continued exciting advances in education, research and clinical services.

All my best for a wonderful year.
Ovarian Cancer Screening: Update and Future

Ovarian cancer meets the World Health Organization’s definition of a disease that would benefit from screening because survival is 70%-90% when the disease is caught in its early stages. Unfortunately, most ovarian cancers (70%-80%) are detected in advanced stages when cure rates are poor. Currently there are no screening strategies that are recommended for average-risk women, and the U.S. Preventive Services Task Force recommends against any ovarian cancer screening at the time of a periodic health exam. Results of the Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial were reported in 2011, and investigators found that yearly screening with transvaginal ultrasound (TVS) and CA125 did not reduce mortality for ovarian cancer. In addition, 15% of women who underwent surgery for false positive screens suffered major surgical complications.

The UK Collaborative Trial of Ovarian Cancer Screening has evaluated serial CA125s to identify upward trends even within the “normal” range. Women with elevated or rising CA125s are then evaluated with TVS. Preliminary results have been promising as a possible effective method of identifying ovarian cancer, but evaluation of results for possible reduction in ovarian cancer mortality is still pending. Also, the algorithm used is quite complex and may be difficult to do outside of a clinical trial.

One of the biggest challenges for ovarian cancer screening is that the incidence in women over 50 is only 30-40/100,000 women. This means that even with a perfect screening test, 2,500 to 3,000 women need to be screened to detect one case of ovarian cancer. Therefore, identifying low-cost methods of screening women at average risk is essential. Recently we have developed a Symptom Index (SI), which has been shown to be predictive of ovarian cancer. The SI is considered positive if women have abdominal or pelvic pain, difficulty eating or feeling full quickly, and bloating or increased abdominal size that occur more than 12 times a month and have been present for less than a year. We are currently conducting a clinical trial of over 6,000 women in primary care clinics who are participating in symptom-triggered screening. Women who screen positive on the SI are then referred for TVS and CA125. Initial results have shown that symptom-triggered screening is acceptable to patients and practitioners, is feasible in primary care settings and is safe, with a false positive rate for major surgery of less than 0.1%. Cancer outcomes are still being assessed.
Biochemical Markers for the Detection of Human Sperm with Failed Development: Advances in the Andrology and Embryology Laboratories

In the past two decades various sperm biomarkers have been identified by the Huszar laboratory, and their role in human sperm fertilizing potential, implantation and pregnancy success has been studied. In the first approach, sperm creatine kinase content and the presence of surplus cytoplasm were assessed, which reflects incomplete sperm cytoplasmic extrusion during spermiogenesis. Indeed, it has been observed that normal spermatozoa that completed cytoplasmic extrusion preferentially bind to the zona pellucida. These experiments provided three conclusions: 1) Sperm that failed to undergo cytoplasmic extrusion (and thus contain excess cytoplasm) are diminished in binding to the zona pellucida. 2) Sperm-oocyte interaction during fertilization is directed and regulated for the most part by the attributes of the spermatozoa. 3) Another key development has been the recognition of the sperm plasma membrane remodeling, simultaneously with cytoplasmic extrusion, in terminal spermiogenesis. This remodeling facilitates the formation of the zona pellucida and hyaluronic acid binding site(s) of sperm. Sperm that fail to undergo the plasma membrane remodeling are unable to recognize the zona pellucida; thus potential for conventional (not ICSI) fertilization of such sperm is diminished. Incomplete cytoplasmic extrusion and plasma membrane remodeling were linked to upstream spermatogenetic and spermiogenetic defects, which may adversely affect chromatin development, DNA integrity and frequency of chromosomal aneuploidies.

Another key biomarker identified in human sperm is the chaperone protein HspA2, which is part of the synaptonemal complex, and also a key element of intracellular transport of DNA repair enzymes and other housekeeping elements in the developing spermatozoa. In the clinical area, the markers of sperm creatine kinase and HspA2 levels were tested with respect to pregnancy success in couples treated with intrauterine insemination. A logical regression analysis demonstrated that elevated or low levels of sperm creatine kinase content predicted the occurrence or failure of pregnancies, independently from sperm concentration and motility. Further, in a blinded collaborative study between the Yale and Norfolk programs, IVF cycles of 82 couples were examined. If the sperm creatine kinase in the husband’s sample was elevated, the couples did not achieve pregnancy. In a similar study, husbands of IVF couples with low sperm HspA2 levels failed to cause pregnancies. In both studies, there were about 15% of men who were normozoospermic with good sperm concentration and motility, yet they did not achieve pregnancy either in the creatine kinase-focused or in the HspA2 chaperone protein-focused IVF group. This is the basis for the idea of the “unexplained male infertility” concept (diminished fertility in spite of normal sperm concentration and motility) that was developed in the Huszar laboratory.

With respect to testing sperm fertilizing potential and ICSI sperm selection via hyaluronic acid-based technology, the scientific basis was
the recognition of sperm plasma membrane remodeling in terminal spermiogenesis. In the presence of hyaluronic acid or hyaluronan, which is well represented in the female reproductive tract, human sperm exhibited a substantially increased tail cross-beat frequency. Further, when solid state hyaluronic acid was applied to a glass slide or a plastic surface, sperm attached to hyaluronic acid headfirst: the sperm progress was stopped secondary to the head attachment, yet the tail-beating frequency increased and was maintained, sometimes even overnight. It was demonstrated that during sperm plasma membrane remodeling, along with the development of zona pellucida receptors, receptors for hyaluronic acid are also formed.

In the andrology diagnostic aspect, hyaluronic acid binding provides an objective measure of semen fertilizing potential, as the proportion of sperm in an ejaculate that binds to hyaluronic acid-coated slides (which represent the zona pellucida, due to the common developmental origin of the zona pellucida and hyaluronan receptors) may be determined in approximately 10 minutes.

Intracytoplasmic sperm injection, or ICSI, had been introduced in the mid ‘90s for treatment of male infertility patients with low sperm concentration and motility. ICSI may also be used in non-oligozoospermic men, those with unexplained male infertility, characterized by normal seminal sperm concentration and motility yet diminished fertilizing potential, identifiable with the sperm biomarkers. Due to the variations of sperm with normal or arrested development, a key issue of ICSI is sperm quality. Regarding ICSI sperm selection, it should be recognized that, due to the historically known incidence of various adverse genetic events, one would prefer to select and use for ICSI sperm that would exhibit properties similar to the sperm that are normally binding to the zona pellucida of oocytes, and thus participate in physiological conception.

The observations regarding the common origin of the zona pellucida and hyaluronic acid receptor led to two inventions: 1) For the first time in the history of andrology, there is now a semen test (in addition to assessment of sperm concentration, motility and morphology), which predicts what percentage of sperm in an ejaculate would have zona binding properties. This is a very important opportunity for physicians and patients. 2) The individual hyaluronic acid-bound spermatozoa are removable with a micropipette and may be used for intracytoplasmic sperm injection. This provides the opportunity to the embryologist to have ICSI fertilization with sperm that normally would have been fertilized under zona pellucida-mediated physiological circumstances during intercourse or IVF. Further studies indicated that hyaluronic acid-bound spermatozoa: (a) are two- to threefold enriched, similar to zona pellucida-bound spermatozoa, in Kruger normal morphology spermatozoa, (b) are devoid of cytoplasmic retention and apoptotic processes, (c) show normally developing chromatin components without persistent histones, (d) exhibit very high sperm DNA integrity, and (e) show normal frequency of chromosomal aneuploidies, no matter how high the aneuploidy and diploidy rates were in the semen sample from which the sperm originate.

In the clinical practice, ICSI performed with hyaluronic acid-selected spermatozoa showed higher fertilization rates, better embryo quality, improved implantation rates, higher pregnancy rates and substantially lower first trimester miscarriage rates. The shape and biochemical properties, as well as genetic attributes of HA-selected sperm, are comparable to that of the zona pellucida-bound sperm. In the past few years, both HA-mediated devices – the sperm hyaluronic acid-binding assessment in the andrology laboratory and the ICSI sperm selection device, the so-called PICSI dish (an IVF Petri dish that carries an HA-spot) – have been increasingly accepted and used worldwide. Indeed, a clinical trial of hyaluronan-based ICSI sperm selection will commence soon in several IVF centers in the UK.
Preventing Unintended Pregnancies by Providing No-Cost Contraception

OBJECTIVE

To promote the use of long-acting reversible contraceptive (LARC) methods (intrauterine devices [IUDs] and implants) and provide contraception at no cost to a large cohort of participants in an effort to reduce unintended pregnancies in our region.

METHODS

We enrolled 9,256 adolescents and women at risk for unintended pregnancy into the Contraceptive CHOICE Project, a prospective cohort study of adolescents and women desiring reversible contraceptive methods. Participants were recruited from the two abortion facilities in the St. Louis region and through provider referral, advertisements and word of mouth. Contraceptive counseling included all reversible methods but emphasized the superior effectiveness of LARC methods (IUDs and implants). All participants received the reversible contraceptive method of their choice at no cost. We analyzed abortion rates, the percentage of abortions that were repeat abortions, and teenage births.

RESULTS

We observed a significant reduction in the percentage of abortions that were repeat abortions in the St. Louis region compared to Kansas City and nonmetropolitan Missouri (p< .001). Abortion rates in the CHOICE cohort were less than half the regional and national rates (p< .001). The rate of teenage births within the CHOICE cohort was 6.3 per 1,000, compared with the U.S. rate of 34.3 per 1,000.

CONCLUSION

We noted a clinically and statistically significant reduction in abortion rates, repeat abortions and teenage birth rates. Unintended pregnancies may be reduced by providing no-cost contraception and promoting the most effective contraceptive methods (1).

LEVEL OF EVIDENCE: II

Unintended pregnancies, pregnancies that are unwanted or mistimed at conception, are a costly public health problem. U.S. taxpayers pay approximately $11 billion annually in costs associated with 1 million unintended births (2). The unintended pregnancy rate in the United States is significantly higher than in other developed countries (3). In the 2006–2008 cycle of the National Survey of Family Growth, 49% of all pregnancies were reported to be unintended. Of these, 29% were mistimed, 19% were unwanted and 43% ended in abortion (4). Approximately half of unintended pregnancies result from nonuse of contraception, and half result from inconsistent or incorrect use and contraceptive failure (5).

Intrauterine devices (IUDs) and contraceptive implants, collectively referred to as long-acting reversible contraceptive (LARC) methods,
are highly effective and safe and have high satisfaction and continuation rates (6). However, these methods are underutilized in the United States. In other developed countries where IUDs are used more frequently, unintended pregnancy rates are lower (7). In fact, in a study examining global rates of unintended pregnancy between 1995 and 2008, North America was the only region of the world that did not see a decrease in the rate of unintended pregnancy (3). The most commonly used reversible contraceptive method in the United States is the oral contraceptive pill (OCP), despite its “typical use” failure rate of 8%–9% per year (8). However, IUDs and implants are more than 20 times more effective at preventing pregnancy than are OCPs, the contraceptive patch and the contraceptive vaginal ring (9).

The objective of the Contraceptive CHOICE Project was to promote the use of LARC methods and to provide no-cost contraception to a large number of women and adolescents in our region in an effort to reduce unintended pregnancies. The primary population-based outcomes for our study were the rate of teen births and the percentage of abortions that are repeat abortions. We also estimated abortion rates in our metropolitan area and in our cohort and compared these rates with U.S. and regional abortion rates.

**PAYMENTS AND METHODS**

We designed a prospective cohort study with two objectives: 1) to promote the use of the most effective contraceptive methods (IUDs and implants) and 2) to provide contraception at no cost to 10,000 female participants in our region who were at risk for unintended pregnancy (10). Before initiating recruitment, we obtained approval from the Washington University Human Research Protection Office.

CHOICE participants met the following inclusion criteria: 1) age 14–45 years, 2) desired reversible contraception, 3) not currently using a method or willing to switch to a new reversible contraceptive method, 4) no desire for pregnancy for at least 12 months, 5) currently sexually active or plan to be sexually active with a male partner within the subsequent next six months, 6) resided in the St. Louis region, and 7) English or Spanish speaking. We excluded potential participants if they were surgically sterile.

CHOICE participants were recruited by provider referral, newspaper reports and advertisements, study flyers and word of mouth. In addition, we recruited eligible participants from local clinics and the two main abortion facilities in our region. All participants received the reversible contraceptive method of their choice at no cost for three years (first 5,090 participants) or two years (remainder of cohort). After completion of the study, participants could continue their IUD or implant because these methods last three years (implant) to 10 years (copper IUD), but could no longer obtain contraception at no cost or change methods as part of the project.

All participants were read a brief script informing them of the effectiveness and safety of LARC methods at initial contact and completed an in-depth, evidence-based contraceptive counseling session at enrollment (11). Participants were offered all U.S. Food and Drug Administration (FDA)-approved contraceptive methods and could choose any method. Each participant provided written informed consent and was monitored prospectively for the duration of follow-up.

Our primary population-based outcomes included teenage births and repeat abortions as proxies for unintended pregnancies. Because participant recruitment sites included two regional abortion facilities, we believed our greatest population effect would be on repeat abortions, or the percentage of abortions that are performed in adolescents and women with a previous abortion. Thus, one of our primary outcomes of interest was the percentage of abortions that were repeat abortions. We compared repeat abortion data in the St. Louis region with that in Kansas City, Missouri, and nonmetropolitan Missouri. Kansas City is of similar size and demographic profile to St. Louis (Table 1).
Although not an *a priori* primary outcome of interest, we also estimated abortion rates because the majority of abortions result from unintended pregnancies. Reproductive Health Services of Planned Parenthood is the major abortion provider in the St. Louis area and represents 90% of the abortions among St. Louis-area females reported to the Missouri Department of Health and Senior Services.

We obtained abortion data from two sources. We obtained the total number of abortions per year among Missouri residents served at Reproductive Health Services, grouped by county-level residence. We also obtained the total number of abortions per year and the number of abortions among females who reported a prior abortion at the time of the current abortion at the state level from the Missouri Department of Health and Senior Services. The Missouri Department of Health and Senior Services also maintains reciprocal vital statistics reporting with other states to obtain information on abortions that occur in Missouri residents at facilities located outside of Missouri. The Missouri Department of Health and Senior Services reported the total and repeat abortion numbers by four geographic locations based on patient ZIP code and grouped by St. Louis City or County (our study catchment area), Kansas City and all remaining ZIP codes grouped as nonmetropolitan Missouri.

Abortion rates among participants aged 15–44 years and births among participants aged 15–19 years within CHOICE were compared with regional and national rates. Because the CHOICE cohort represents a higher-risk population (median age of 25 years and 50% black) than the general population, we standardized the CHOICE abortion rate to the age and racial (black and white) distribution of females who reside in the St. Louis region, using data from the 2010 U.S. Census (direct standardization). We compared the CHOICE standardized rate with the St. Louis regional rate using data from the Missouri Department of Health and Senior Services and with the national rate using the most recent published data from 2008 (12).

Statistical analyses were performed using STATA software. The significance level was set at 0.05. Means, standard deviations, frequencies and percentages were used to describe the demographic characteristics of the study
participants. We calculated 95% confidence intervals around the percentage of abortions that were repeat for each year from 2006 through 2010. We used a Pearson X² to determine a significant difference in the proportion of repeat abortions each year between the St. Louis region and Kansas City, and a Mantel-Haenszel score test for trend of odds of repeat abortions for 2006–2010 for the St. Louis, Kansas City and nonmetropolitan Missouri regions, individually. We used negative binomial regression models to estimate the time trend for total abortions in the St. Louis region and in non-St. Louis, Missouri. We estimated the population-attributable risk by calculating the risk difference between CHOICE and the St. Louis region rates and multiplying by the St. Louis region population divided by 1,000, and we calculated the number needed to treat by taking the inverse of the absolute risk reduction. Confidence intervals for the number needed to treat were estimated using the Bender method (13).

For sample size calculations, we considered a 50%–60% reduction within the study population or a 6%–7% St. Louis region reduction in teen births (baseline rate 39 per 1,000 15–19-year-old females) and repeat abortion (baseline rate 430 per 1,000 abortions) to be of clinical and public health significance. Further, we assumed no change in the remainder of the St. Louis population not participating in the study, an alpha of 0.05 and a power of 80%. Our intent was to interact with 11% of the population in the region at greatest risk for unintended pregnancy. Further, we estimated that 10% of the cohort would choose an IUD and 3% of the cohort would choose an implant, a rate almost double that of current IUD and implant use in the United States in 2008 (8). Based on these assumptions, an enrollment of 2,000 participants aged 15–19 years would represent 11% of the population at risk for teenage pregnancy, and an enrollment of 5,000 participants with a history of abortion would reach 11% of the population at risk of repeat abortion. The uptake of IUD and implant was much greater than originally predicted (10), leading to greater observed reductions in pregnancy risk among the accrued study population than anticipated, and allowing us to exceed our initial targets for population effect.

RESULTS

Between August 2007 and September 2011, 9,256 adolescents and women enrolled in CHOICE; of these participants, 16% were recruited at the abortion facilities. The baseline demographic and reproductive characteristics of the cohort are provided in Table 2. The mean age of the total population was 25 years; 51% were black, 35% had a high school education or less, 37% received public assistance and 39% had trouble paying for basic expenses. Forty-seven percent were nulliparous; 63% had a prior unintended pregnancy. Participants chose the following contraceptive methods at baseline: 46% levonorgestrel IUD, 12% copper IUD, 17% subdermal implant, 9% OCPs, 7% contraceptive vaginal ring, 7% depot medroxyprogesterone acetate and 2% contraceptive patch. Thus, 75% of our study population chose a LARC method.

Participants recruited at the abortion clinics were more likely to be black and to report a high school education or less, trouble paying for basic necessities, receipt of public assistance or no insurance, greater parity and a history of three or more unintended pregnancies. We also found that these participants were more likely to choose a LARC method at enrollment compared with adolescents and women enrolled at the other recruitment clinics (84.5% compared with 72.9%, p<.001).

We evaluated teenage birth (births per 1,000 females aged 15–19) as a proxy for unintended pregnancy because up to 80% of these births are unintended (4, 14). The number of teenage births in the United States has decreased markedly in the past several years, with a 44% drop between 1991 and 2010 to a level of 34.3 per 1,000 (15). The birth rate among participants aged 15–19 years within the CHOICE cohort was 6.3 per 1,000, a rate far below the national level.

Figure 1 shows the number of abortions among
Missouri residents reported by Reproductive Health Services, stratified by region (St. Louis City and County and compared with the rest of Missouri). Between 2008 and 2010, the number of abortions performed at Reproductive Health Services among women and teenagers who resided in St. Louis City and County declined by 20.6% (p<.001), compared with no appreciable change (0%, p=.39) in the number of abortions among women and teenagers who resided in the rest of Missouri.

Our primary outcome of interest was the percentage of abortions that were repeat abortions for the following reasons: 1) this information is tracked by providers and in government statistics and 2) our objective was to have the maximum population effect through the provision of our intervention to participants at highest risk for unintended pregnancy. Women and teenagers seeking pregnancy terminations are at risk for future unintended pregnancy and repeat abortion as well as potentially motivated to seek contraceptive services. Using vital statistics data from the state health department, Figure 2 shows a significant difference in the proportion of repeat abortions between the St. Louis region and Kansas City in 2009 (p=.02) and 2010 (p<.01). We also detected a significant decline in the proportion of repeat abortions over time in the St. Louis region (p=.002).

![Figure 2. Number of abortions in Missouri residents reported by Reproductive Health Services, 2006–2010. P for test of trend over time: St. Louis City and County, P<.001; all other Missouri residents, P=.39.](image-url)
Between 2008 and 2010, abortion rates in CHOICE participants ranged from 4.4 to 7.5 per 1,000 after adjusting for age and race (Table 3). These rates are considerably less than the rates in St. Louis City and County for the same years (p<.001) and far below the national rate of 19.6 per 1,000. Using these data, we then estimated the difference in abortion rates and number of abortions prevented each year if CHOICE were available to the entire population of the region. Based on the number needed to treat, one abortion could be prevented for every 79–137 women and teenagers provided the CHOICE intervention.

**DISCUSSION**

The Institute of Medicine recently recommended that eight primary preventive health services for women be covered without cost to patients under the Patient Protection and Affordable Care Act of 2010 (16). Among these eight services, the Institute of Medicine recommended “a fuller range of contraceptive education, counseling, methods and services so that women can better avoid unwanted pregnancies and space their pregnancies to promote optimal birth outcomes.” As a result, all FDA-approved contraceptive methods would be covered without cost. The Contraceptive CHOICE Project essentially simulated this recommendation in our region for reversible contraceptive methods. All women received any FDA-approved contraceptive method of their choice as well as having the ability to change methods at no cost. In addition, the project provided education to promote the use of the most effective contraceptive methods, IUDs and implants in an effort to alter population outcomes.

There are few studies that have investigated whether increasing the uptake of LARC methods decreases unintended pregnancy. A recent analysis of the family planning expansion program in California, known as the Family Planning, Access, Care and Treatment Program, examined the association between increased contraceptive access and unintended pregnancy (17). Using a Markov model, the authors estimated that increasing contraceptive access to low-income women averted more than 286,000 unintended pregnancies. Interestingly, uptake of LARC was substantially lower among Family Planning, Access, Care and Treatment Program participants than among CHOICE participants; however, the increased access to no-cost contraception still resulted in a significant reduction in the number of unintended pregnancies. A qualitative study of women undergoing abortion found that there was a high level of interest in LARC methods for post-abortion contraception, but the majority of women also identified cost as a barrier to obtaining a LARC method (18). Participation in CHOICE provided participants with access to IUDs and implants that they otherwise might not have had, including teenagers and women recently post-abortion who are at high risk for repeat unintended pregnancy.

The birth rate for females 15–19 years of age in our cohort is markedly less than the U.S. rate despite a remarkable decline in teenage births nationally (15). We also noted a substantially lower abortion rate in our cohort compared with regional and national statistics, and a significant decline in repeat abortions in the St. Louis region. Increasing access to the most effective contraceptive methods by removing cost and
Access as barriers has greatly increased the number of adolescents and women in the St. Louis region using the most effective methods of birth control. Providing no-cost contraception and promoting the use of highly effective contraceptive methods have the potential to reduce unintended pregnancies in the United States. In fact, based on our calculations in Table 3, changes in contraceptive policy simulating the Contraceptive CHOICE Project would prevent as many as 62% to 78% of abortions performed annually in the United States.

Table 3. Abortion Rates per 1,000 Women and Adolescents in CHOICE, St. Louis, and the United States and Estimated Population Effect of the Contraceptive CHOICE Project

<table>
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<tr>
<th>Year</th>
<th>CHOICE Rate</th>
<th>Region Rate</th>
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<td>Rate†</td>
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<td>133</td>
</tr>
</tbody>
</table>

NNT, number needed to treat; CI, confidence interval; NA, not applicable.
* Among black and white females, aged 15–44, adjusting for age and race using 2010 U.S. Census data.
† Among black and white females, aged 15–44, denominator is 2010 U.S. Census data.
‡ CHOICE compared with St. Louis rate, number of abortions prevented in St. Louis City or County.
§ CHOICE compared with St. Louis rate, number needed to treat to prevent one abortion.

Another limitation is that the analysis comparing repeat abortion in the St. Louis region with that in Kansas City and nonmetropolitan Missouri is essentially an ecological study. There may be several factors that affect the rates of repeat abortion, such as the economic recession, federal changes in Title X funding for family planning, and Missouri state laws that limit access to abortion. It is not possible to conclude that the changes observed in repeat abortion were due solely to the Contraceptive CHOICE Project. However, the weight of the evidence, including a marked reduction in teenage births and abortion rates compared with regional and national statistics, provides the existence of a population effect of the CHOICE intervention.

Intendedness of pregnancy is not captured in the state vital statistics; therefore, we used proxy markers of unintended pregnancy. The strengths of our study include the prospective design of the Contraceptive CHOICE Project (a large sample with a high uptake of the most effective contraceptive methods), the use of systematically collected state-mandated data, and partnership with community clinics serving adolescents and women at highest risk for unintended pregnancy. Our study also has several limitations. Intendedness of pregnancy remains a stubborn problem in the United States, with higher proportions among adolescents and young women, racial and ethnic minorities, and women with less education and lower socioeconomic status (4). Approximately half of unintended pregnancies are the result of contraceptive failure (21), with the majority of women using reversible contraception such as OCPs or condoms (8). The American College of Obstetricians and Gynecologists and many family planning experts believe that LARC methods should be first-line
contraceptive options and that increased uptake of LARC methods is essential to decreasing the rate of unintended pregnancy (22-24). In addition, because LARC methods have been shown to have higher continuation rates than other reversible methods, the number of adolescents using no contraception would decline, further decreasing the unintended pregnancy rate (6). Increased access to contraception, particularly highly effective LARC methods, and providing contraception at no cost may result in a significant decrease in the rate of unintended pregnancy in the United States.
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Evidence-Based Breastfeeding Promotion: The Baby Friendly Hospital Initiative

INTRODUCTION

The strong public health benefits that breastfeeding offers to children and women worldwide have led the World Health Organization (WHO), UNICEF and the American Academy of Pediatrics to strongly endorse this behavior (1, 2). One of the most successful global initiatives designed to promote optimal breastfeeding behaviors is the Baby Friendly Hospital Initiative (BFHI) (3), otherwise known as the Baby Friendly Initiative (BFI) in the USA. The BFHI was launched in 1991 by WHO and UNICEF to support the implementation of the 1990 Innocenti Declaration on the need to protect, promote and support breastfeeding (4), which, among other things, calls for the implementation and enforcement of the 1981 WHO Code for the Marketing of Breast Milk Substitutes (5). Hospitals and clinics offering maternity services can obtain the Baby Friendly designation if they follow 10 steps (Figure 1) as attested by a well-structured external evaluation procedure (3).

The 10 BFHI steps call for: facilities to have written breastfeeding policies, healthcare personnel to be adequately trained, women to receive breastfeeding education and support starting prenatally, breastfeeding to be initiated within a half hour after birth, all mothers who choose to breastfeed to receive breastfeeding counseling and support in the maternity ward, breast milk to be the sole source of feeding for newborns, mothers and newborns to room-in throughout the hospital stay, breastfeeding on-demand, not using baby bottles or pacifiers, and facilitating community-based breastfeeding support once the dyad is discharged from the maternity ward. Thus, BFHI represents a comprehensive strategy based on policy, training, lactation management support and appropriate infrastructure to facilitate the breastfeeding process. UNICEF and WHO have developed well-structured BFHI training manuals targeting both maternity staff (6) and decision makers (7). This has facilitated its global spread and scaling up. Indeed, the BFHI is one of the most successful...
maternal-child global health initiatives, at least when it comes to dissemination. As of October 2012, there were over 20,000 facilities in 152 countries with the Baby Friendly designation (8). However, of these only 149 are located in the USA, representing a mere 5.8% of facilities offering maternity services in the country (9).

Given the global spread of BFHI, a key question is whether this initiative has had demonstrable impacts on breastfeeding and child health outcomes. Thus, the main objectives of this Grand Rounds paper are to review: a) the efficacy, effectiveness and cost-effectiveness evidence behind the BFHI and b) the role that BFHI has played in successful national breastfeeding programs.

EFFICACY AND EFFECTIVENESS

Pérez-Escamilla et al. conducted a global systematic review in the early ‘90s to assess the impact of BFHI steps at improving breastfeeding outcomes (10). They identified 18 experimental or quasi-experimental studies that met the review’s inclusion criteria. A meta-analysis suggested that receiving free formula samples at hospital discharge was a significant risk factor for the early discontinuation of breastfeeding. Based on a single quasi-experimental study, this review concluded that rooming-in had a short-term impact on breastfeeding success, but this impact was sustained in the longer term only in the presence of lactation support in the maternity ward. The review also documented that at the time the BFHI was launched, there was practically no evidence to help understand the impact of the rest of the BFHI steps alone or in combination.

The first study that examined the impact of the BFHI “package” on exclusive breastfeeding (EBF) duration was conducted in Santos, Brazil (11). In this study participants delivered in either a hospital serving low-income women where all BFHI steps were being strongly enforced or in another close-by hospital serving women of similar socioeconomic status where mothers roomed-in with their newborns and formula was not widely available but the rest of the BFHI steps had not been implemented. EBF duration was 3.5 times higher among women delivering in the BFHI hospital vs. their counterparts delivering in the comparison hospital (Figure 2). Those women who wanted to deliver in the BFHI hospital but ended up doing so in the comparison hospital because the former was full had EBF durations that were similar to the rest of the sample from the comparison ward.

Figure 2

These findings were replicated in the PROBIT-Belarus randomized controlled trial (RCT) (12) where infants who were born in BFHI facilities and served by their associated polyclinics after hospital discharge were 6.8 times more likely to be exclusively breastfed vs. those who were born in the control hospitals where none of the BFHI steps had been implemented. BFHI also had a positive impact on the prevalence of any breastfeeding at 12 months postpartum (Figure 3). This trial also documented that BFHI reduced the incidence of gastrointestinal infections (9.1% vs. 13.2%) and atopic eczema (3.3% vs. 6.6%). In this study children from the BFHI group had higher IQ scores when they were 6.5 years old compared to their counterparts born in the control hospitals (13).
COST-EFFECTIVENESS

The study conducted in Santos, Brazil, was replicated in Mexico City and two cities in Honduras (14). A stronger BFHI implementation was associated with improved breastfeeding outcomes in all three countries. These improvements were translated into economic savings estimates based on the predicted protective effect of breastfeeding against childhood gastrointestinal and upper respiratory diseases. These studies also obtained detailed primary data on costs associated with initial implementation and sustainability of BFHI. An in-depth economic analysis found that BFHI was highly cost-effective, comparing favorably against other interventions that are considered highly cost-effective, including immunizations, vitamin A supplementation and tuberculosis therapy (15).

COMMUNITY-BASED SUPPORT

Given the short stay after delivery in maternity wards, especially for uncomplicated vaginal deliveries, BFHI’s step 10 (link with community-level support) is crucial for successful breastfeeding programs. Unfortunately, this is a step that tends to be very weakly implemented despite knowing how to effectively support breastfeeding at the community level.

Efficacy of community-based breastfeeding support

Morrow and colleagues (16) randomly assigned pregnant women from a low-income neighborhood in Mexico City to high-intensity peer counseling, low-intensity peer counseling or a control group. The high-intensity group received six home visits from trained peer counselors in early and late pregnancy as well as during the first eight weeks postpartum. The low-intensity group received three peer counseling visits: one in late pregnancy and two during the first two weeks postpartum. The control group did not receive any visits from peer counselors. The study documented a dose response relationship, with women in the high-intensity group being 5.6 times and those in the low-intensity group being 4.2 times more likely than their counterparts in the control group to be EBF at 12 weeks postpartum (Figure 4). In this study, the cumulative incidence of infant diarrhea was 12% in the peer counseling groups vs. 26% in the control group. The findings by Morrow et al. were subsequently replicated in South Asia and the Middle East (17). However, whether this approach could work in Sub-Saharan Africa remained unknown until an RCT was conducted in Ghana to assess the impact of home-based breastfeeding support by public health nurses on EBF (18). Pregnant women recruited at prenatal care clinics were randomly assigned to either: a) receive home support pre- and postnatally
and also postpartum breastfeeding support in the maternity ward; b) receive home support only postnatally and postpartum breastfeeding support in the maternity ward; or c) receive health education unrelated to breastfeeding at home visits and in the maternity ward. The latter group allowed for adjusting for contact time with the public health nurses and thus to account for the Hawthorne effect. This community-based support intervention, with or without the prenatal care component, led to a doubling of the rates of EBF throughout the first six months postpartum (40% in intervention groups combined vs. 20% in the control group) (18). The findings from the Ghanaian study have now been replicated in Sub-Saharan Africa by the large-scale PROMISE-EBF clustered RCT (19) that recently reported major improvements in EBF rates in Burkina Faso and Uganda. But, interestingly enough, this study found that baseline and absolute increases in EBF rates in South Africa were exceptionally low, very likely as a result of the widespread availability of free infant formula to low-income women in violation of the 1981 WHO Code.

Anderson et al. (20) conducted the first RCT examining the efficacy of EBF peer counseling in the USA. This RCT targeted a low-income sample of predominantly Latina women who were receiving prenatal care at an inner-city Baby Friendly hospital in Hartford, Connecticut. Women were randomly assigned to the standard of care control group or to the intervention group that in addition received three prenatal home visits, additional breastfeeding perinatal support in the maternity ward and postpartum home visits during the first six weeks after birth. The study’s breastfeeding peer counselor was a Latina woman who had successfully breastfed her children and who received extensive training on EBF promotion. The intervention had a strong impact on increasing EBF rates (Figure 5). The intervention also led to a significant reduction in the incidence of infant diarrhea at three months and in the proportion of women who remained amenorrheic at three months (Figure 6).

A second RCT conducted by Chapman et al. (21) in the same community targeted obese women and found that in this instance the efficacy of the intervention was limited to only short-term breastfeeding outcomes but interestingly led to a reduction in the rate of infant hospitalization during the first three months of life.

In summary, studies conducted in diverse socioeconomic and cultural environments strongly support the efficacy of peer counseling at improving breastfeeding and child health outcomes. The question then becomes if this approach is effective in the “real world.”

**Effectiveness of community-based breastfeeding support**

Dearden et al. (22) examined the association between a breastfeeding peer counseling training
program and EBF rates in a disadvantaged peri-urban area of Guatemala City. This program involved high-quality training of unpaid female volunteers from the target communities who were then assigned to facilitate support groups, conduct home visits and have informal contact with women to support breastfeeding in their neighborhoods. A cross-sectional survey targeting women with infants under six months living in intervention and control communities found that the training program had no impact on improving EBF rates (Figure 7). This is likely explained by the very low coverage that the program had, as only 21% of women received a home visit and only 16% participated in a support group in the intervention communities. As expected, based on the efficacy evidence presented in the previous section, women who were actually exposed to the peer counseling support did have significantly higher EBF rates following a dose–response pattern (Figure 8).

An effectiveness RCT conducted in Hartford, Connecticut, also found that a real-world breastfeeding peer counseling program had a positive but modest impact on improving any breastfeeding initiation and duration. These impacts were significantly weaker than those documented by Anderson et al. (20) in the efficacy trial targeting the same population.

**NATIONAL BREASTFEEDING PROGRAMS**

A recent global systematic review of barriers and facilitators for successful scaling up and sustainability of national breastfeeding programs in low- and middle-income countries, where less than a third of infants under six months are exclusively breastfed (23), led to the development of the “Breastfeeding Gear” model (24). Analogous to a well-oiled engine, this model posits that the key gears needed for successful large-scale breastfeeding programs are: a) evidence-based advocacy, b) political will, c) policy and legislation (e.g., paid maternity leave of adequate duration, breastfeeding or breast milk extraction breaks during the workday, implementation and enforcement of the 1981 WHO Code), d) fiscal and infrastructural resources, e) training and implementation of facility-based and community-based breastfeeding promotion and support, f) social communication campaigns and events (e.g., mass media, breastfeeding week) and g) research and evaluation. For these gears to function properly and move at the right pace, a central or master gear is needed to provide specific goals, monitor progress and provide timely multidirectional feedback into the gear systems (24, 25). The master gear needs to be run by an intersectoral team and to allow for adequate coordination from the municipal to the national level based on a participatory and transparent governance structure.

**CONCLUSIONS**

BFHI and community-based peer counseling are highly efficacious at improving breastfeeding
and child health outcomes. Research conducted in Latin America strongly supports the cost-effectiveness of BFHI in low- and middle-income countries. Observational studies from the U.S., Canada and other developed countries (26-29) also support the effectiveness of BFHI. Likewise, experimental studies in developed nations also support the efficacy of community-based peer counseling programs in developed countries (17).

BFHI has been a central component for successful national breastfeeding programs. However, it is only one of several key components needed for the programs to work effectively in the real world. Although the “Breastfeeding Gear” model was developed based on evidence from low- and middle-income countries, it is likely to be valid in the U.S. context also. Indeed, the recent USA Surgeon General’s call to action to support breastfeeding (30, 31) can be easily mapped into this scaling-up model.

It is crucial to reinvigorate BFHI globally as part of a well-planned strategy to improve breastfeeding and infant health outcomes. Urgent action is particularly needed in the USA where, despite breastfeeding having been deemed cost-effective (32), less than 6% of maternity hospitals have been certified as Baby Friendly, EBF rates and any breastfeeding duration remain very low, breastfeeding is not the social norm and unethical marketing from infant formula continues to be widespread and unchallenged (33-35). The time has indeed come for translating the strong evidence base for effective ways to protect, promote and support breastfeeding into large-scale action in the USA for the well-being of our women, children, families and society as a whole (34, 35).
REFERENCES


Reliability of Laparoscopic Compared to Hysteroscopic Sterilization at One Year: A Decision Analysis

INTRODUCTION

Female sterilization is one of the most commonly used methods of contraception. Of the 38.2 million United States women using a contraceptive from 2006-2008, 27% utilized female sterilization (1). While this proportion has been stable since 1988, the methods employed to achieve sterilization have changed (2).

Hysteroscopic sterilization (HS) has been commercially available since 2002. Advantages of HS include that it is a non-incisional method, avoids abdominal entry (which may be especially important in women with adhesions or co-morbidities), can be performed as an office procedure and avoids general anesthesia. A six-year review of sterilization trends at a United States academic medical center from 2002-2006 showed a 50% decline in both laparoscopic sterilization (LS) and postpartum sterilizations and a corresponding 50% increase in HS (3). According to the manufacturer of Essure®, the most popular HS system, approximately 310,000 devices have been placed as of 2010 (4).

However, unlike LS, which conveys immediate reliability, HS is a multi-step process in which the HS procedure is followed by a confirmatory hysterosalpingogram (HSG) performed at least three months after the initial procedure to prove bilateral tubal occlusion before women can rely on this method of contraception (5). For women without occlusion but with devices present, an additional HSG may be indicated three months later. Alternative contraception must be used until occlusion is proven. Each step of this process introduces a chance of finding that the procedure failed, of non-compliance with use of alternative contraception or loss to follow-up. Failed attempts at HS can subject women to multiple procedures, cause a delay in achieving sterilization and increase the risk of unintended pregnancy.

Current published assessments of HS success do not adequately address these complex issues. Reported success rates often exclude women who failed initial microinsert placement or did not return for HSG, thereby falsely elevating the percentages of successful sterilization. Accordingly, we performed an evidence-based decision analysis that includes these complexities in order to better estimate the likelihood of a successful sterilization procedure after HS or LS.

MATERIALS AND METHODS

We developed an evidence-based Markov decision model (Figure 1) to compare the probability of a successful sterilization procedure via three strategies: LS, HS in the operating room (OR) and HS in the office setting. The Markov model, using monthly cycles, contains health states and transition probabilities between those states corresponding to differing paths that could occur with each strategy, including the probabilities of successful sterilization, of follow-up procedures (and their outcomes) and of proceeding with alternative procedures (and their success) if prior procedures were unsuccessful.
The primary objective of the model was to estimate the probability of successful sterilization after HS or LS based on available data. HS and LS success was defined in accordance with standard clinical practice. A successful HS procedure was defined as having bilateral blockage of fallopian tubes on follow-up HSG evaluation. A successful LS procedure was defined as physical obstruction of the fallopian tubes at the time of surgery.

For the model, women were maintained in groups based on the original attempted procedure. Thus, women in HS strategies who ultimately received LS were counted as an HS success, biasing against the LS strategy. Cohorts were followed for one year. Standard decision-analysis software was used (TreeAge Pro Suite 2009).

Procedure and follow-up testing probabilities were estimated from published sources (Table 1). This model used data pertaining to Essure® HS only, due to its dominance of the market. The major sources for base case values (and the ranges of lowest and highest reasonable values) were identified through a comprehensive literature search of all pertinent studies in English in PubMed and Ovid (last searched April 13, 2011) and by reviewing the bibliographies of identified references. All published studies that reported more than 50 subjects were included. However, some studies did not provide complete information for every outcome in the model. The base case values and ranges used in the model, as well as the studies referenced to provide this information, are described in Table 1. The values themselves are a mathematical average of the results from the referenced studies. When data were missing from published literature, we used data from our own practice’s active database, which was initiated in July 2003. Outcome data from studies that did not evaluate the success of HS using HSG, as required by the U.S. Food and Drug Administration (FDA), were not included in this analysis.

Follow-up rates of HSG at three months vary widely (Table 1), with the highest follow-up rates reported in the original HS clinical trials performed by the manufacturer. The base case
<table>
<thead>
<tr>
<th>Probabilities of:</th>
<th>Baseline Value</th>
<th>Range</th>
<th>Reference or Assumption</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Laparoscopic Sterilization</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Successful LS</td>
<td>99%-100%</td>
<td>99%-100%</td>
<td>6, 7</td>
</tr>
<tr>
<td>Choose HS in OR if LS failed</td>
<td>20%</td>
<td>10%-50%</td>
<td>Expert opinion</td>
</tr>
<tr>
<td>Major complication</td>
<td>1%</td>
<td>0.098%-1.7%</td>
<td>7-11</td>
</tr>
<tr>
<td>Minor complication</td>
<td>0.5%</td>
<td>0.26%-1%</td>
<td>10, 11</td>
</tr>
<tr>
<td>Probability of death</td>
<td>0%</td>
<td></td>
<td>7, 8, 11</td>
</tr>
<tr>
<td><strong>HS in OR</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Successful coil placement on first attempt</td>
<td>90%</td>
<td>85%-95%</td>
<td>12-19</td>
</tr>
<tr>
<td>Major complication</td>
<td>0.13%</td>
<td>0%-0.4%</td>
<td>12, 14, 16</td>
</tr>
<tr>
<td>Minor complication</td>
<td>5%</td>
<td>4%-7%</td>
<td>12-14, 16</td>
</tr>
<tr>
<td>Choose second OR procedure</td>
<td>70%</td>
<td>41%-100%</td>
<td>13, 17-19</td>
</tr>
<tr>
<td>Choose LS after one failed HS in OR</td>
<td>83%</td>
<td>67%-100%</td>
<td>13, 17-19</td>
</tr>
<tr>
<td>Successful coil placement on second attempt</td>
<td>84%</td>
<td>67%-100%</td>
<td>12, 13, 17, 19</td>
</tr>
<tr>
<td>Probability of death</td>
<td>0%</td>
<td></td>
<td>12</td>
</tr>
<tr>
<td><strong>HS in Office</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Successful coil placement on first HS attempt</td>
<td>90%</td>
<td>76%-96%</td>
<td>6, 15, 20-23</td>
</tr>
<tr>
<td>Major complication</td>
<td>0%</td>
<td></td>
<td>20, 24, 25</td>
</tr>
<tr>
<td>Minor complication</td>
<td>5%</td>
<td>2%-8%</td>
<td>20, 24, 25</td>
</tr>
<tr>
<td>Choose second procedure after one failed</td>
<td>70%</td>
<td>21%-100%</td>
<td>6, 20, 24</td>
</tr>
<tr>
<td>Choose HS</td>
<td>33%</td>
<td>0%-67%</td>
<td>20, 24</td>
</tr>
<tr>
<td>Successful coil placement on second attempt</td>
<td>80%</td>
<td>67%-100%</td>
<td>6, 20, 22</td>
</tr>
<tr>
<td>Probability of death</td>
<td>0%</td>
<td></td>
<td>15</td>
</tr>
<tr>
<td><strong>HSG Outcomes</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Returning for HSG at three months</td>
<td>69%</td>
<td>13%-94%</td>
<td>6, 13, 18, 21, 23, 24</td>
</tr>
<tr>
<td>HSG: Coils present</td>
<td>97%</td>
<td>95%-99%</td>
<td>12, 14, 16, 24</td>
</tr>
<tr>
<td>HSG: Blockage at three months</td>
<td>96%</td>
<td>84%-100%</td>
<td>6, 12-14, 16, 21, 23, 24</td>
</tr>
<tr>
<td>Returning for HSG at six months</td>
<td>69%</td>
<td>13%-94%</td>
<td>Assume same as for three months</td>
</tr>
<tr>
<td>HSG: Blockage at six months</td>
<td>98%</td>
<td>93%-100%</td>
<td>12-14, 24</td>
</tr>
<tr>
<td>Assumed sterile if do not return for HSG</td>
<td>96%</td>
<td>84%-99%</td>
<td>Assume same as for women who do return at three and six months</td>
</tr>
</tbody>
</table>

**If HSG at three months shows non-occlusion**

*Initial procedure in OR*

| Choosing another procedure         | 30%            |             | Practice database       |
| Choosing second HS in OR           | 50%            |             | Practice database       |
| Occlusion with second HS in OR     | 73%            | 45%-100%    | 16, Practice             |
values used in this analysis were limited to subsequent case series or cohort analyses in an effort to avoid bias. However, we did include the manufacturer’s follow-up rates of 98% to 100% in the sensitivity analyses (12, 14, 16).

In the absence of published data, the following assumptions were made for the model:

- 20% of women who failed LS would accept HS;
- probability of choosing another HS procedure after one failed HS (defined as a negative HSG) would be the same after HS performed in the OR or office;
- probability of choosing a repeat HS procedure (as opposed to choosing an LS procedure) after a failed HS in the office (defined as a negative HSG) would be the same as is reported for the OR;
- second HS had similar success regardless of operating room or office location;
- probability of returning for HSG at six months is similar to the probability at three months;
- would not want a third HS attempt.

HS success was identical whether or not women completed follow-up testing.

A schematic diagram of the Markov model is shown in Figure 1. Sterilization via LS, HS in the operating room and HS in the office setting were tested in identical hypothetical cohorts of women. Complications related to HS and LS are also included in the model, but are not shown in Figure 1.

Using published data, the model also calculates the number of women who pursue a second or third attempt after a failed sterilization and the number of women who stop pursuing sterilization after one failed attempt.

One-way sensitivity analysis was performed for the reasonable range of values identified for all parameters.

**RESULTS**

In the base case analysis, the percentage of women able to rely on their method of sterilization at three months post-procedure (without having any other procedures done) is 99% for LS, 86% for HS in OR and 85% for HS in office. The reliance rate at six months post-procedure (without having any other procedures done) is 99%, 88% and 87%, respectively.

The probability of having any successful sterilization procedure within one year is 99% for women starting with LS, 95% for women starting with HS in the operating room and 94% for women starting with HS in the office. However, the method by which the woman was ultimately sterilized sometimes differs from the method initially chosen. In the base case analysis, 7.0% and 5.3% of women who undergo an initial HS procedure in the operating room or office, respectively, actually achieve sterilization via LS. Of the women who experienced one failed attempt at an HS procedure, approximately 5% will decline any further sterilization attempts.

In sensitivity analyses, we found that the model is most strongly influenced by the high probability of success with LS (Figure 2). However, even if the model is biased against LS by using the highest probability of success for HS (97.9% for HS in operating room and 97.2% for HS in office) and the lowest probability of success for LS (98.3%), we found that LS would still outperform HS and 0.4% more women would have successful sterilization procedures if they initially chose LS. In contrast, if we use the highest probability of success for LS (99.6%) and the lowest for HS (89.5% for HS in office), the difference in successful sterilization procedures within one year is as large as 10%.
DISCUSSION

Women seeking permanent sterilization deserve an accurate assessment of the likelihood of success for both HS and LS. The time required to achieve sterilization before women can rely on it must also be included as part of the informed consent process. According to this model, 85% to 86% of women who chose HS will have a successful sterilization procedure by three months. This finding is consistent with the results from the Essure® pivotal clinical trial (26).

By 12 months, 95% of women who chose HS in the operating room will have a successful sterilization procedure. However, the additional percentage gained by one year is mostly due to subsequent successful sterilization via LS. Seven percent of women choosing HS in the OR and 5% of women choosing HS in the office will ultimately require LS to be sterilized, and may only reach their goal of sterilization after multiple attempts at microinsert placement, HSGs, office visits, time missed from work, insurance co-pays and the need for other reliable interim contraception.

In the base case analysis, the large majority of women choosing HS in the office or operating room will have a successful sterilization procedure. However, women choosing HS are less likely to have a successful sterilization procedure than women choosing LS. In this analysis, the difference in success rates between the two approaches could be as large as 10%, although the true difference will vary by patient population.

In the United States, 345,000 women undergo sterilization annually (1). If all female sterilizations in the United States were performed only by HS, this model predicts that approximately 31,050 women would not achieve actual sterilization within one year of their initial HS procedure. This estimate is comprised of the 5% of women who experience one failed attempt at HS and decline any further sterilization attempts and the 4% of women (99% minus 95%) who do not achieve sterilization by HS as compared to those choosing LS.

Failed attempts at sterilization can result in unintended pregnancies. In a recent analysis of outcomes after unfulfilled postpartum sterilization, the risk of pregnancy within one year was twice that of women not requesting sterilization (27).

Failed sterilizations resulting in unintended pregnancy can also occur after a successful procedure. Data on pregnancy after successful HS is reported to be zero by the manufacturer of Essure® and is currently limited to case reports. For LS, the CREST (Collaborative Review of Sterilization) study showed a cumulative pregnancy rate at one year of 0.68% (28). At one year, if we assume a pregnancy rate of zero after HS and 0.68% after LS, the likelihood of being able to rely on sterilization is still lower with HS than with LS.

The Adiana system, another multi-step method of hysteroscopic sterilization, was approved by the FDA in 2009. In the pivotal clinical trial for Adiana, the number of patients able to ultimately rely on Adiana at one year after placement was similar to that reported for Essure® (29). Thus, the findings of this model are likely applicable to Adiana.

This model and its findings are limited by the uncertainty of the data they are based on. The biggest limitation of published HS data is that the majority comes from observational case series or cohort designs and there is a lack of any randomized trials directly comparing HS and LS (30). Published studies are also limited by low follow-up rates and possible conflicts of
interest since most HS studies are performed by the manufacturer (12, 16). Also, we could not incorporate the results of five years of post-approval data collection that were presented by the manufacturer to the FDA in the spring of 2010 as they have not been published (as of PubMed and Ovid search April 13, 2011).

Limitations with published LS data do not take into account women who were never offered LS due to co-morbid conditions that were relative contraindications for general anesthesia or Trendelenburg positioning required for LS, or due to knowledge of significant adhesive disease. While the same argument could be applied to women who weren’t offered HS, the absolute and relative contraindications to HS are less frequently encountered than for LS.

However, contraindications to HS may be difficult to identify preoperatively. According to the package insert, Essure® should not be used for any patient “for whom only one microinsert can be placed (including patients with apparent contralateral proximal tubal occlusion and patients with a suspected unicornuate uterus)” (31). Uterine anomalies and tubal scarring are often asymptomatic.

Comparative trials are needed to assess true long-term efficacy and costs of HS. Reported success rates for HS that exclude patients who failed bilateral microinsert placement, failed to return for HSG or were ultimately sterilized by LS are disingenuous. For physicians and patients, reporting of HS success rates must include the actual number of women who can truly rely on the method for its desired effect. We plan further analyses to evaluate cost and comparative pregnancy rates over time to provide additional data for women and their providers.
REFERENCES


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Prognostic Factors and Treatment-Related Outcomes in Patients with Uterine Serous Cancer (USC)

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BACKGROUND
Uterine cancer is the most common gynecologic cancer in the United States. In 2011 there were an estimated 47,000 new cases and 8,000 deaths. Uterine serous cancer (USC) is a type II uterine cancer that is uncommon (10%) but aggressive, and reported to cause 50% of all uterine cancer deaths. Because of its low incidence, there is a lack of specific treatment guidelines, leading to variations in treatment management of patients. The goal of this study is to report the largest single-institution experience with USC in order to identify prognostic factors and report clinical outcomes based on pathologic findings and treatment approaches. The primary end points for this study are five-year overall survival (OS) and five-year disease-free survival (DFS).

METHODS
A total of 334 patients with USC were included in this retrospective study. All patients were surgically staged at Yale-New Haven Hospital between the years 1987 and 2009. Medical records and pathology reports were reviewed. Patients were followed from date of diagnosis to last clinic visit or date of death. For patients who relapsed, the site of tumor recurrence was also reviewed. Disease stage was based on FIGO 2009 uterine cancer staging. Postoperative management strategies were observation (OBS, n=33), platinum-based chemotherapy (PCH, n=78), whole abdominal radiation therapy (WART, n=16), PCH and vaginal apex brachytherapy (PCHR, n=165) and vaginal apex brachytherapy (VAB, n=35). Primary outcome was overall survival and disease-free survival. The Kaplan-Meier method was used to generate five-year OS and five-year DFS data. Cox regression analysis was used to compare clinical factors that impact OS and DFS.

RESULTS
The mean age at diagnosis was 69 years (range 37-92). The mean follow-up was 73 months (range 1-290). Past medical history revealed 177 of 221 (80%) had HTN, 69 of 221 (32%) had DM and 132 of 292 (45.3%) were obese with BMI >30. There were 121 patients with stage IA disease (36.2%), 36 stage IB (10.8%), 27 stage II (8.1%), 39 stage IIIA (11.7%), 2 stage IIIB (0.6%), 32 stage IIIC1 (9.6%), 9 stage IIIC2 (2.7%), 28 stage IVA (8.4%) and 40 stage IVB (12%). For treatment-related outcomes, the five-year OS for stage IA/IB disease was 94% for patients who received PCHR, 90% for OBS, 75% for PCH, 65% for VAB and 0% for WART. The five-year DFS percentages for PCHR, OBS, PCH, VAB and WART for Stage IA/IB were 89%, 82%, 86%, 72% and 0%, respectively. For stage II-IVB patients, the five-year OS was 51% for PCHR, 0% for OBS, 23% for PCH and 20% for WART. The five-year DFS percentages for stage II-IVB with PCHR, OBS, PCH and WART were 42%, 0%, 17% and 13%, respectively. Advanced stage was associated with significantly shorter OS and DFS (p<0.01). Older age patients had worse survival (p<0.01). Race and BMI did not impact survival. Incomplete surgical debulking (p<0.01), depth of myometrial invasion >50% (p<0.01) and lymph node metastasis (p<0.01) were all associated with worse prognosis. Among all patients, those who received chemotherapy and radiation (vaginal apex or pelvic radiation) had longer OS compared to those who did not receive chemotherapy.
CONCLUSION

Successful management of USC patients requires complete surgical staging and postoperative chemoradiation. In addition, our data show that USC patients share demographic features such as obesity, hypertension and diabetes that are routinely found in the more common low-grade endometrioid adenocarcinoma of the endometrium.
Neoadjuvant Chemotherapy (NACT) Is an Effective Way of Managing Elderly Women with Advanced Stage Ovarian Cancer (FIGO Stage IIIIC and IV)

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BACKGROUND

Neoadjuvant chemotherapy (NACT) is an alternative treatment approach to primary cytoreductive surgery for the management of advanced epithelial ovarian cancer. NACT involves the administration of cytotoxic chemotherapy prior to aggressive cytoreductive surgery. Several studies have suggested that NACT offers women the possibility of a greater chance of optimal debulking with less surgical morbidity compared with primary cytoreductive surgery. The aim of this study was to compare outcomes in women ≥ age 70 who receive NACT for advanced epithelial ovarian cancer (EOC) followed by cytoreductive surgery with those undergoing upfront cytoreductive surgery followed by the same chemotherapy.

METHODS

A retrospective cohort study was performed for women ≥ age 70 with stage IIIC or stage IV EOC from 1996 to 2009. Patients were identified through the gynecologic oncology tumor board database, and disease status was confirmed through the hospital-based tumor registry. Demographic and clinical data were abstracted from individual inpatient and outpatient records as well as operative and pathological reports.

RESULTS

Sixty-two patients who underwent upfront cytoreductive surgery and 42 patients who received NACT were eligible for analysis. Patients receiving NACT were significantly more likely to have stage IV disease (p=0.004). Cytoreduction to no macroscopic disease was achieved in 71.4% of women who received NACT and 28.1% of women undergoing upfront surgery (p<0.001). NACT patients had significantly less blood loss at surgery (p=0.01), required fewer small bowel resections (p=0.009) and had shorter ICU stays (p=0.02) and fewer hospital days (p=0.04). NACT patients experienced a trend toward an improved progression-free survival (p=0.078); however, no statistically significant differences were found in either the progression-free or overall survival analyses.

CONCLUSION

NACT is associated with reduced perioperative morbidity in elderly patients with advanced-stage ovarian cancer. The survival was the same as with upfront cytoreductive surgery.
Teaching Basic Ultrasound Skills at Mulago Hospital, Kampala, Uganda

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Makerere University School of Medicine and Health Sciences, Department of Obstetrics and Gynecology, Mulago Hospital, Kampala, Uganda

BACKGROUND

Mulago Hospital is a referral hospital located on the outskirts of the city center that is also a teaching hospital under the Makerere University School of Medicine and Health Sciences. The labor and delivery unit had nearly 31,000 deliveries occurring there in 2009. Basic ultrasound skills are useful in the assessment and management of obstetric patients. The purpose of the study is to assess the effectiveness of a teaching intervention (via pre- and post-test survey) that will be implemented to teach basic ultrasound skills, such as identification of fetal lie, placental position, amniotic fluid volume assessment and recognition of fetal breathing and motion, to residents, interns and medical students at Mulago Hospital, Kampala, Uganda.

METHODS

The teaching intervention includes a combination of didactic methods and demonstration of skills, about one to two hours in total length. Each participant completed a pre- and post-survey to assess their knowledge and skills. Data was analyzed in Microsoft Excel and SAS software.

RESULTS

On average, scores between the pre- and post-test improved by 1.6 times for all participants (n=37, p=0.001). Participants included 12 medical students, 21 interns and 4 residents. Scores of medical students and interns improved more significantly, 2.3 times (p<0.001) and 2.0 times (p<0.001), respectively, than scores of residents (1.2 times, p=0.30).

CONCLUSION

This original teaching intervention was an effective method to improve knowledge and skills for medical students and interns at Mulago Hospital in the area of basic obstetric ultrasound.
Robotic-Assisted Surgical Staging for Uterine Cancer: What Have We Learned at Yale?

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BACKGROUND

The International Federation of Gynecology and Obstetrics (FIGO) maintains that a total extrafascial hysterectomy and bilateral salpingo-oopherectomy with pelvic and para-aortic lymph node dissection is the standard staging procedure for endometrial cancer. The da Vinci Surgical System was approved by the U.S. Food and Drug Administration (FDA) for use in gynecologic procedures in 2005 and has been shown to have several advantages over traditional laparoscopy, including a three-dimensional field of vision, instruments with a wrist-like range of motion, tremor filtration, a superior ergonomic profile and a faster learning curve. Robotic surgery has been rapidly and widely adopted in gynecologic oncology as it was shown to be safe and to facilitate performing complex procedures such as retroperitoneal lymph node dissection.

When compared to laparotomy, robotic staging has been associated with a decrease in operative blood loss, fewer perioperative complications, shorter hospital stay and faster return to normal activity with no significant difference in lymph node yield or operative cost but an increase in operative time. When compared to traditional laparoscopy, robotic-assisted staging for endometrial cancer seems to be more effective in patients with an elevated BMI and has been associated with a decrease in operative time, blood loss and length of postoperative stay in obese patients, with no significant difference in lymph node yield or operative cost. In this study we reviewed the Yale experience of robotic-assisted surgical staging for endometrial cancer.

METHODS

Retrospective chart review of patients with uterine cancer for whom surgical staging was performed robotically. Demographic, operative, pathology and postoperative clinical data were obtained for consecutive patients undergoing surgery at Yale-New Haven Hospital and Bridgeport Hospital between October 2006 and August 2011. Collected information included age, stage, histology and American Society of Anesthesiologists (ASA) classification, which served as a marker of preoperative risk as well as intra-operative complications and postoperative complications occurring within 30 days of surgical staging that either required further workup or affected a patient’s postoperative course. Use of an intrauterine manipulator at the time of surgical staging, as well as evidence of lymphovascular space invasion (LVI), was also evaluated.

RESULTS

Preliminary results revealed a mean patient age of 62.4 years. Mean body mass index was 34.5 Kg/m2. Mean operative time was 127 minutes. Mean lymph node count was 20.3. Mean estimated blood loss was 119 ml. Mean hospital stay was 1.5 days. Eighty-one percent of patients had early (stage I or II) disease and 81% of patients were found to have endometrioid histology. The incidences of postoperative ileus (0.6%), infections (5.2%), anemia/transfusion of blood products (1.3%) and cardiopulmonary complications (3.2%) were comparable to those previously reported. There was one postoperative death, which was attributed to the patient’s preexisting cardiac condition. There was no statistical difference noted in LVI and the cytology of pelvic washings between patients who had an intrauterine manipulator placed during surgical staging and those who did not.

CONCLUSION

Robotic-assisted surgery is an appropriate and safe approach for uterine cancer staging in patients. Our preliminary data at Yale suggest that patients with a spectrum of preoperative co-morbidities and BMIs can be offered
robotic staging and expect comparable initial postoperative outcomes. Operative time, which has been shown to be the significant detractor for robotic surgery when compared to traditional laparoscopy, can be decreased with increased operator experience and a dedicated robotic surgical team. There is ongoing controversy about whether use of an intrauterine manipulator increases the risk of seeding malignant cells into the lymphovascular or intraperitoneal space. Preliminary data at our institution do not suggest that use of an intrauterine manipulator increases these risks.
Uroplakin IIIb Expression in Endometrium from Patients with Endometriosis

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ABSTRACT

Uroplakins are the protein building blocks of urothelial plaques that act as a barrier along the urothelium and affect permeability, secretion and absorption of proteins and biochemicals. We have identified Uroplakin III (UPKIII) as a target of HOXA10 in murine endometrium using microarray analysis, generating our interest in Uroplakin III expression within human endometrium. Prior to this work, uroplakin expression was thought to be limited to the bladder. Endometrial samples were collected from 10 patients with and without endometriosis in the mid-secretory phase under an approved HIC protocol. Normal human endometrium expresses small amounts of UPKIII protein as demonstrated by immunohistochemistry. Endometrium from patients with endometriosis expresses a fourfold (p<0.001) higher level of UPKIII mRNA compared to normal controls. In this study, we demonstrate that UPKIII is a downstream target of HOXA10 expression in human endometrium, and UPKIII expression is significantly upregulated in endometrial cells from patients with endometriosis. This finding is of importance in that overexpression of UPKIII may function as a new barrier to implantation in patients with endometriosis.

METHODS

The case-control study included 20 subjects: 10 patients with endometriosis and 10 patients without endometriosis. All subjects were undergoing laparoscopy for diagnostic evaluation of pelvic pain. Eutopic and ectopic endometrium were collected from patients with endometriosis (n=10) and patients without endometriosis (n=10). Endometrial Uroplakin IIIb protein expression was evaluated with immunohistochemistry, in vivo gene transfection and tissue microarray.

RESULTS

Immunohistochemical results reveal higher UPKIII expression in endometrium from patients with endometriosis compared to controls. To identify putative genes regulated by HOXA10, we performed an initial screen of these targets employing a microarray. When HOXA10 was overexpressed, the microarray results demonstrated an almost 2.9-fold decrease in UPKIII mRNA expression. There was a statistically significant higher level of UPKIII mRNA noted in eutopic and ectopic endometrium from patients with endometriosis compared to the samples from normal healthy patients (p<0.01). Compared with controls, endometrial UPKIII mRNA expression (normalized to ß-actin expression) was significantly increased in eutopic endometrial biopsies from patients with endometriosis (1.42 and 6.18, respectively; p<0.05).

CONCLUSION

Inadequate uterine receptivity is responsible for approximately two thirds of implantation failures, whereas the embryo itself is responsible for only one third of these. The data suggest that alterations in HOX genes can produce a cascade of additional defects in the expression of downstream target genes. Whether this defect is inherent to the eutopic endometrium or the result of other factors associated with endometriosis remains to be demonstrated. A better understanding of the mechanisms regulating embryo implantation may improve infertility treatments for patients with endometriosis, prevent early pregnancy loss and develop new contraceptive approaches.
Identification of Putative Fallopian Tube Progenitor Stem Cells

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OBJECTIVE

The endometrium has remarkable ability to regenerate and repair after each injury or menses. We have previously shown that stem cells play a significant role in mediating endometrial repair and tissue regeneration. Here we identify label-retaining cells (LRCs) in the murine oviduct that suggest the presence of a progenitor stem cell population in this tissue.

STUDY DESIGN

This is an in vivo murine study.

MATERIALS AND METHOD

CD-1 mice were housed in standard conditions with food and water provided ad libitum at a constant light cycle of 12 hours. Ethics approval for this project was granted by the Yale University Institutional Animal Care and Use Committee. Two-day-old mice were injected intraperitoneally with 5-bromo-2-deoxyuridine (BrdU) at a dose of 50μg/g body weight while the control group received sterile water. Female animals (n=12 for each group) were sacrificed at 4, 5 and 6 weeks post-injection. Reproductive tracts were removed, washed in normal saline and then placed in 10% formaldehyde solution. Specimens were embedded in paraffin and 5 micron sections were prepared. Oviduct was identified by H+E staining and morphology. Immunofluorescence (IF) studies were performed on serial section tissues (n=12 per animal) using antibodies against BrdU (Abcam). DAPI was used to identify nuclei. In the negative controls, primary antibody was substituted with non-specific IgG. Confocal microscopy was used to identify DAPI and BrdU stained nuclei.

RESULTS

In the group of mice exposed to BrdU, we identified a population of LRCs in all specimens. These cells were localized mainly at the base of the fallopian tube villi. Four random high-power fields (HPFs) were counted on each of 12 slides from 12 animals (576 HPFs). The number of LRCs was divided by the number of DAPI stained nuclei; LRCs constituted 0.5% of all nuclei. The control groups (saline-treated animals examined with the primary antibody and BrdU-treated animals examined without the primary antibody) were negative.

CONCLUSION

The murine endometrium is known for its remarkable regenerative capacity as it undergoes dynamic changes each estrous cycle, but there is limited research investigating the processes of regeneration of the fallopian tube. In the oviduct we identified label-retaining cells characteristic of progenitor stem cells. The fallopian tube, like endometrium, contains a population of progenitor cells. The stem cells are located at the base of each villus, suggesting the location of the stem cell niche. These stem cells likely are used in the repair and regeneration of the fallopian tube.
Differential Responses to Toll-Like Receptor (TLR) Ligands in Hofbauer Cells (HBCs), Placental Fibroblasts (FIBs) and Human Umbilical Vein Endothelial Cells (HUVECs): Implications for the Genesis of Fetal Inflammatory Response Syndrome (FIRS)

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OBJECTIVE

Acute chorioamnionitis and chronic inflammation have been implicated in dysfunctional neuronal migration and as contributors to the onset of FIRS and cerebral palsy. However, little is known as to how various cell types in the placental villus core and umbilical cord respond to a microbial challenge. The objective of this study is to elucidate the patterns of microbial-driven pro-inflammatory processes in HBCs (i.e., placental macrophages), FIBs and HUVECs in order to gain insight into the mechanism of FIRS.

STUDY DESIGN

HBCs, FIBs and HUVECs were cultured in a medium containing 10% fetal bovine serum (FBS) or in a serum-free medium for 24 hours or 48 hours with and without lipopolysaccharide (LPS: a TLR-4 ligand), peptidoglycan (PG: a TLR-2 ligand), polyinosinic:polycytidylic acid (PIC: a TLR-3 ligand) and LPS binding protein (LPS-BP: a TLR-4 co-activator). Levels of mRNA for IL-6, IL-8 and tissue factor (TF), all factors whose expression is known to increase in FIRS, were measured by quantitative real-time polymerase chain reaction (qRT-PCR) and normalized to 18S RNA expression. Levels of IL-6 and IL-8 in conditioned media were measured by enzyme-linked immunoabsorbent assay (ELISA) and normalized to cell protein. Statistical analysis was performed using Sigma Stat software.

RESULTS

HBCs, when stimulated with LPS, demonstrated significant IL-6 mRNA and protein expression (p<0.05) was noted in all three cell types in response to LPS; however, the extent of mRNA and expression in both FIBs and HUVECs far exceeded that seen in HBCs. Notably, any mRNA or protein expression of both IL-6 and IL-8 in FIBs and HUVECs required supplementation with LPS-BP, but not in HBCs. TF mRNA expression was markedly induced by approximately 100-fold (p<0.05) in both HBCs and HUVECs but not in FIBs. In all cell types, the degree of induction of all three cytokines in response to PG and PIC was much less prominent than that seen in response to LPS.

CONCLUSION

LPS treatment of HBCs produced the most significant effects on levels of IL-6, suggesting a role of this cell type in the FIRS cascade. The requirement of LPS-BP for any cytokine expression in the presence of LPS in both FIBs and HUVECs indicates the necessity of TLR-4 co-activation in these two cell types. Such cell-specific TLR-mediated cytokine expression in all cells of the placental villus core and of the umbilical cord indicates the complexity of the initiation of FIRS.
ABSTRACTS FROM RECENT SCIENTIFIC MEETINGS

Yale Oral and Poster Presentations at the Society of Gynecologic Oncologists 44th Annual Meeting, March 9-12, 2013, Los Angeles, California

POSTER PRESENTATIONS


ABSTRACTS FROM RECENT SCIENTIFIC MEETINGS


ORAL PRESENTATIONS


POSTER PRESENTATIONS


ABSTRACTS FROM RECENT SCIENTIFIC MEETINGS


ORAL PRESENTATIONS


Relevance of “Scots’ Paradox” for Reproductive Biology? L. Pal, N. Kidwai, W. Grant.

The Association Between Assisted Reproductive Technology (ART) Clinic Success Rates and Number of Embryos Transferred Per Cycle. D. Gong, E. Seli.


Vitamin D (VitD) Status Predicts PCOS Related Infertility Treatment Success: Retrospective Cohort Analysis of 25OHD Levels in Stored SERA from an RCT of Clomid (CC) vs. Metformin (M) vs. (CC+M) in PCOS. L. Pal, J. Williams.


Lyophilized and Rehydrated Metaphase II (MII) Ovine Chromosomes Maintain Functionality upon Transfer in Fresh MII Oocytes. P. Loi, D. Iuso, G. Ptak, P. Patrizio, A. Arav.

POSTER PRESENTATIONS


Increasing FSH Dosage Beyond Physiological Range Fails to Upregulate Estradiol Production by Granulosa Cells In Vitro. M.D. Lalioti, E. Seli, T. Gerasimova.


ABSTRACTS FROM RECENT SCIENTIFIC MEETINGS

Yale Oral and Poster Presentations at the Society for Gynecologic Investigation 60th Annual Meeting, March 20-23, 2013, Orlando, Florida

ORAL PRESENTATIONS


*Recipient of the Pfizer President’s Presenter Award


*Recipient of the Pfizer President’s Presenter Award


Human Endometrial Endothelial Cells Generate an Inflammatory and Anti-Viral Response to the TLR3 Agonist, Poly(I:C). G. Krikun, J. Potter, S. Guller, G. Mor, V.M. Abrahams.

Glucocorticoid Treatment Enhances Hemoglobin Scavenging by Fetal Hofbauer Cells Through a CD163-Dependent Mechanism. S. Guller, Z. Tang.

POSTER PRESENTATIONS


*Treatment with Bazedoxifene and Conjugated Estrogens Results in Regression of Murine Experimental Endometriosis. H. Naqvi, S. Sakr, T. Presti, G. Krikun, B. Auerbach, H.S. Taylor.

Bazedoxifene Treatment Decreases Expression of BRCA2 in Mouse Mammary Gland. C. Fischer, J. Kulak, L. Mutlu, B. Komm, H.S. Taylor.


Genome-Wide Methylation Profile Identifies Genes Involved in the Pathogenesis of Endometriosis. H. Naqvi, H.S. Taylor.


Hydroxychloroquine Prevents Antiphospholipid Antibody-Induced Inhibition of Trophoblast Migration. C.R. Albert, M.J. Mulla, C.S. Han, J.J. Brosens, L.W. Chamley, V.M. Abrahams.

Fetal Membranes Generate Distinct Cytokine Profiles in Response to Different Bacterial Toll-Like and Nod-Like Receptor Agonists. M. Hoang, J.A. Potter, C.S. Han, S. Guller, E.R. Norwitz, V.M. Abrahams.

Role of Caspase-1 in Fetal Membrane IL-1 Production in Response to Bacterial Toll-Like Receptor and Nod Protein Agonists. M. Hoang, J.A. Potter, C.S. Han, S. Guller, E.R. Norwitz, V.M. Abrahams.


H19 IncRNA-Mediated Regulation of Gene Expression in Granulosa Cells. A. Kallen, J. Ma, Y. Huang.


Metformin Reverses Hyperglycemia-Induced Upregulation of IL-6 Secretion by Human First Trimester Trophoblast. M.C. Pitruzzello, J. Hastie, M.A. Herrin, C. Flannery, E.F. Werner, V.M. Abrahams, C.S. Han.


First Trimester Decidual Cells Mediate Pro-Inflammatory-Induced M1 Macrophage Polarization-Implication in Preeclampsia. M. Li, C. Chen, C. Yeh, S. Pels, S.J. Huang.


Endometrial Stromal Stem Cells from Women with Endometriosis Abnormally Express COX-2, StAR, CYP19A1 and Apoptotic Markers. G. Krikun, B. Kadalmani, K. Palanivel, H.S. Taylor.
ABSTRACTS FROM RECENT SCIENTIFIC MEETINGS


ORAL PRESENTATIONS

School-Age Outcomes of Late Preterm Infants by Delivery Indication. H. Lipkind, M. Slopen, K. McVeigh.

POSTER PRESENTATIONS

Decreased Expression of Endostatin (ES) and Hypoxia-Inducible Factor 1A (HIF-1A) Is Associated with Excessive Trophoblast Invasion and Aberrant Angiogenesis in Placenta Accreta. C.M. Duzyj, I.A. Buhimschi, J.T. Hardy, M.E. McCarthy, G. Zhao, S.N. Cross, T.J. Rutherford, M.P. Bahtiyar, C.S. Buhimschi.


Recombinant Human antithrombin (rHaT) for Prevention of Venous Thromboembolism (VTE) in Pregnant Patients with Hereditary Antithrombin Deficiency (HD). M. Paidas, E. Triche, A. James, T. Ballard, S. Lowry.


WELCOME TO OUR NEW OB/GYN INTERNS

We are pleased to announce the interns for 2012-2013. All seven are outstanding and highly accomplished physicians.

GARY ALTWERGER, MD – University at Buffalo State University of New York School of Medicine & Biomedical Sciences

Gary received his BS (Biochemistry, Molecular Biology) at State University at Albany. He was the recipient of the Dean’s Letter of Commendation in 2008 and 2009. He extended his medical education training for a year when he was accepted into the Clinical Research Training Program (CRTP), a program supported by the National Institutes of Health and the Foundation for NIH. His specific translational research project focused on overexpressed proteins in patients with recurrent ovarian carcinoma. Throughout medical school, Gary was involved in a number of volunteer and research projects. His publications include two peer-reviewed journal articles/abstracts and one poster presentation. Gary has a wide range of hobbies and interests, which include playing guitar, sailing, fishing, cross-country skiing and golfing.

KIMBERLY KEEFE, MD – New York University School of Medicine

Kimberly received her BA (Social Anthropology) from Harvard College. In 2010 she received the Biomedical Research Career Award and took a year off during her medical education training to do research with the Reproductive Endocrine Department at Massachusetts General Hospital. Her research project focused on genetic, clinical and biochemical characterization of GnRH deficiency. She is a member of several honorary/professional societies and has been involved in a number of volunteer and research projects during medical school. Her publications include one peer-reviewed article, three poster presentations and two oral presentations. Kimberly’s hobbies and interests include tennis, rowing, soccer, singing, travel and reading.

DEVIN MILLER, MD – Virginia Commonwealth University School of Medicine

Devin received her BS (Kinesiology, Neuroscience) at the College of William and Mary. She is a member of several honorary/professional societies. Devin was elected to participate on numerous committees during medical school, which included the Medicine Curriculum Council, Admissions Committee, Medical Student Government Committee and Honor Council. In one of her research projects, she assisted the project manager with IRB and grant proposals for research on rapid repeat pregnancy in Richmond, Virginia. Devin has a wide range of hobbies and interests, including fitness, cooking, travel, piano, writing and reading.
MASARU NEGI, MD – The School of Medicine at Stony Brook University Medical Center

Masaru received his BA (Economics/Mathematics) at Columbia University. After graduation, Masaru worked as a full-time computer support consultant at Columbia University. He was quickly promoted to applications systems, where he was a lead developer for an issue tracking system, web development and multiple other development projects before deciding to attend medical school. Masaru has been actively involved in numerous volunteer projects throughout undergraduate and medical school, one of which involved volunteering at the Stony Brook HOME Clinic, triaging patients. He was also a paid teaching assistant for a gross anatomy course guiding students through difficult dissections, held office hours, arranged a practice practical exam and ran review sessions. He was inducted into the Alpha Omega Alpha Honor Society at Stony Brook Medical Center as a junior student. Masaru speaks fluent Japanese. His hobbies and interests include guitar, reading and travel.

AMY OSBORNE, MD – Saint James School of Medicine, Netherlands Antilles

Amy received her BS (Animal Biology) at the University of British Columbia and her AS (Midwifery) at the National College of Midwifery. As one of her numerous volunteer projects, Amy spent two weeks in Haiti during the cholera outbreak where she ran a temporary cholera ward in the unused portions of a local hospital. In 2003 she spent several months in Afghanistan, working in a large village as a midwife while training local women as birth attendants, and in 2004 set up a midwifery clinic in Tabuk, Philippines. Amy has an article in the University of British Columbia student newspaper, as well as five oral presentations. She speaks French at a conversational level. Amy’s hobbies and interests include traveling, writing, photography, reading, working overseas, sailing and snowboarding.

MONICA PASTERNAK, MD, MBA – University of Miami Leonard M. Miller School of Medicine

Monica received her BA (Middle Eastern and Asian Languages and Cultures, Biology) at Columbia University and her MBA (Healthcare Public Policy and Administration) at the University of Miami School of Business. She was involved with numerous research and volunteer projects. Currently she is working with Dr. Ruben Quintero, assisting in assimilating and analyzing data for a prospective fetoscopic research investigation aimed at comparing surgical interventions versus expectant management, undertaken secondary to the potential of morbidity and mortality arising from twin-to-twin transfusion syndrome and selective intrauterine growth restriction. She has one peer-reviewed article/abstract. Monica is proficient in both French and Spanish. She has many outside interests including tennis, swimming, skiing, running and golf. She also plays the violin and is an avid reader.
Lissa received her BA (Psychology) at Yale University. She was involved with numerous research and volunteer projects. She is the founder and coordinator of the Reproductive Health Outreach Project/Mobile Clinic that was developed to facilitate a weekly program for medical and public health student volunteers, teaching reproductive health to homeless youths at a local HIV testing and treatment center. She also organized the UCLA Mobile Clinic Project and coordinated other weekly medical clinic sites for homeless and indigent populations. Lissa has one peer-reviewed journal article/abstract, three poster presentations and one oral presentation. She speaks fluent Mandarin Chinese. Lissa’s hobbies include piano, viola, painting, photography, dance and traveling.
Our 2012 Residency Program Graduates and Their Next Destinations

**MARIA DE LEON**  
Gynecologic Oncology Fellowship  
Indiana University School of Medicine

**Michele Glasgow**  
Pelvic Surgery Fellowship  
Emory University

**HOMA KHORRAMI**  
Maternal-Fetal Medicine Fellowship  
Duke University

**RHODA RAJI**  
Surgical Critical Care Fellowship  
University of Texas, Houston

**ANITA SARGENT**  
Private Practice  
Binghamton, New York

**VICTORIA SNEGORSKIKH**  
Reproductive Endocrinology & Infertility Fellowship  
Brown University

**OMAR YOUNG**  
Maternal-Fetal Medicine Fellowship  
Magee-Women’s Hospital
YALE OBSTETRICAL AND GYNECOLOGICAL SOCIETY

Newest Additions to the Yale Faculty

Michelle Silasi, MD, joins the faculty of the Yale Section of Maternal-Fetal Medicine as an Assistant Professor. Michelle obtained her medical degree from the University of Texas Health Sciences Center at San Antonio, Texas. She completed an obstetrics and gynecology residency training program at Women and Infants Hospital/The Warren Alpert Medical School of Brown University in Rhode Island. Dr. Silasi’s MFM fellowship training was at the Beth Israel Deaconess Medical Center in Boston.

Dr. Silasi’s academic interests are related to the study of the pathogenesis of preeclampsia and the role of infection in pregnancy. Her studies have focused on the mechanisms of regulatory molecules in normal compared to preeclamptic placentas. She will expand her interests in collaboration with Dr. Gil Mor and Dr. Catalin Buhimschi on the role of infection as an etiologic factor in preterm labor. Her clinical interests also include maternal medical complications of pregnancy, prenatal diagnosis and the use of biomarkers in the triage of clinical management for patients with preeclampsia.

Katherine Campbell, MD, MPH, joins the faculty of the Yale Section of Maternal-Fetal Medicine as an Assistant Professor of Obstetrics, Gynecology and Reproductive Sciences at Yale School of Medicine. She obtained her medical degree at Michigan State University with distinction before completing an Ob/Gyn residency at Yale-New Haven Hospital where she served as administrative chief resident. She then pursued fellowships in Perinatal Ultrasound and in Maternal-Fetal Medicine at Yale University before joining the Yale faculty. Dr. Campbell has been honored with several awards for her excellence in teaching medical students and residents.

Dr. Campbell is board certified in Obstetrics and Gynecology. She has published numerous peer-reviewed manuscripts related to obstetrical ultrasound and fetal assessment. Her clinical interests include prenatal diagnosis, twin gestations, abnormal placentation and preterm labor.

Nicole Kummer, MD, joins the faculty of Yale Fertility Center as an Assistant Professor. Nicole was an outstanding Ob/Gyn resident at Yale from 2005 to 2009. She obtained her medical degree at Chicago Medical School before completing an Ob/Gyn residency at Yale-New Haven Hospital. She then pursued a fellowship in Reproductive Endocrinology and Infertility at the University of Connecticut before joining the Yale faculty. Dr. Kummer has earned several awards for her excellence in teaching medical students and residents.

Dr. Kummer is board certified in Obstetrics and Gynecology and board eligible in Reproductive Endocrinology and Infertility. She has published numerous peer-reviewed manuscripts related to infertility and controlled ovarian stimulation. Her clinical interests include polycystic ovarian syndrome, recurrent pregnancy loss and infertility treatment.
Newest Additions to the Yale Faculty

**Linda Fan, MD**, joins Yale as Assistant Professor in the section of the Women’s Center in the Division of Gynecology in the Department of Obstetrics, Gynecology and Reproductive Sciences. Dr. Fan obtained her medical degree from Columbia University College of Physicians and Surgeons and her residency training in obstetrics and gynecology at New York-Presbyterian Hospital. Dr. Fan received additional training in minimally invasive surgery, pelvic reconstruction and incontinence at New York-Presbyterian Hospital.

**Clare Flannery, MD**, has joined Yale as Assistant Professor in the section of Reproductive Endocrinology and Infertility in the Department of Obstetrics, Gynecology and Reproductive Sciences. Dr. Flannery will head a new interdisciplinary program in endocrinology. She will also help to establish a multispecialty clinic focused on the reproductive effects of metabolic disease and diabetes; clinical conditions to be treated include polycystic ovary syndrome, gestational diabetes and obesity. She will also conduct research on the effects of insulin on the reproductive tract and fetus.

Dr. Flannery obtained her MB and BCh, BAO from Trinity College of Medicine in Ireland. Her residency training in internal medicine was obtained from Jacobi Medical Center/Albert Einstein College of Medicine. She subsequently moved to the Division of Endocrinology at Yale as a clinical fellow and then postdoctoral research fellow in the Department of Medicine. Dr. Flannery recently received an NIH K12 award to study the effects of insulin on estrogen receptor alpha activity in human endometrium.
New Fellows On Board July 1, 2012

**Gynecologic Oncology**

Diana English, MD

**Reproductive Endocrinology & Infertility**

Sanaz Ghazal, MD

**Maternal-Fetal Medicine**

Sarah Cross, MD  
Andrea Johnson, MD  
Ciprian Gheorghe, MD, PhD

**Urogynecology & Reconstructive Pelvic Surgery**

AeuMuro Lake, MD
Our 2012 Fellowship Graduates and Their Next Destinations

Unzila Ali Nayeri, MD
SUNY Upstate Medical University, Syracuse, New York

Katherine Campbell, MD
Yale University School of Medicine, New Haven, Connecticut

Christine Laky, MD
Carl R. Darnall Army Medical Center, Fort Hood, Texas

Janelle Luk, MD
New Hope Fertility Center, New York, New York

Christine Richter, MD
Munich, Germany

Sallis Yip, MD
Kaiser Permanente, Fontana, California
PHOTO HIGHLIGHTS FROM THE MAY 2012 ALUMNI REUNION IN NEW HAVEN, CONNECTICUT
PHOTO HIGHLIGHTS FROM THE MAY 2012 ALUMNI REUNION IN NEW HAVEN, CONNECTICUT
PHOTO HIGHLIGHTS FROM THE 2012 C. LEE BUXTON RESIDENTS’ RESEARCH DAY
PHOTO HIGHLIGHTS FROM THE 2012 C. LEE BUXTON RESIDENTS’ RESEARCH DAY
HONORING ROBERTO ROMERO, M.D., D.MED.SCI.

Chief, Perinatology Research Branch
Program Director for Perinatal Research and Obstetrics
Division of Intramural Research
NICHD/NIH/DHHS

Dr. Roberto Romero completed his residency in Obstetrics and Gynecology at Yale-New Haven Hospital/Yale University, followed by one year devoted to Gynecologic Oncology and the Physiology of the Uterine Cervix, before pursuing a Fellowship in Maternal-Fetal Medicine. He then joined the faculty and became the first Director of Perinatal Research at Yale before moving to Michigan to accept a position as Professor and Vice Chair of Obstetrics and Gynecology at Wayne State University, along with Chief of the Perinatology Research Branch (a new Branch of NICHD/NIH), a position that he has held for the last 20 years.

Early in his career, Roberto was interested in the diagnosis of ectopic pregnancy (the discriminatory hCG zone, serial hCG titers, culdocentesis and ultrasound), the use of biomarkers in patients with ovarian cancer, and the biochemistry of cervical ripening. As part of the Perinatal Unit, he contributed to the prenatal diagnosis of congenital anomalies with ultrasound (the “Red Book”) and premature labor – these studies led to his interest in intra-amniotic infection, the discovery of the role of cytokines in labor and the fetal inflammatory response syndrome.

Under Roberto’s leadership, the Perinatology Research Branch uses a multidisciplinary approach to address the problems of pregnancy complications. Obstetricians work side-by-side with neonatologists, placental pathologists, epidemiologists, immunologists, computational biologists, microbiologists and geneticists to develop methods to diagnose, treat and prevent complications of pregnancy.

Author of more than 850 peer-reviewed publications, Roberto has been recognized with multiple national (SMFM, SGI, ACOG) and international awards, including the Ian Donald Gold Medal for contributions in ultrasound (Stockholm), the Erich Salting Perinatal Prize (Osaka) and the Maternite Prize (Paris), among many others. He is a member of the Institute of Medicine of the National Academies of the United States and has received several Doctorates Honoris Causa from universities worldwide.

Roberto has maintained strong ties with Yale through research collaborations within and outside our Department, visits for Residents’ Research Day, participation in many YOGS events to honor former distinguished alumni, and long-lasting friendships with many of the voluntary faculty at Yale-New Haven Hospital.
Professor Walter Herrmann, former Director of the Department of Obstetrics and Gynecology of the Maternity Hospital of Geneva, passed away on August 16, 2012, in his 90th year, following an illness that he faced with courage and an exemplary lucidity.

Professor Herrmann did not want any funeral ceremony, but we want to honor him and describe in a few words his many talents and how he influenced the evolution of our medical specialty.

Walter Herrmann was born in 1923 in Berlin. In 1933, his provident father left Germany to settle in Switzerland. It is in Basle and Ticino that Walter Herrmann continued his education. Subsequently, he obtained his medical degree from the University of Geneva and specialized in gynecology and obstetrics in St. Gallen and Zürich.

In 1951 he went to the United States to continue his medical education in the prestigious universities of Harvard, Columbia and Yale, where he acquired an international reputation in his specialty of gynecological endocrinology and sterility.

Following his outstanding scientific career, he was appointed Professor and Chairman of the Department of Obstetrics and Gynecology at the University of Washington in Seattle. He continued his research and teaching in a very challenging academic setting. In his free time, he enjoyed also the incredible diverse nature of the State of Washington.

In 1976 he was called to Geneva to take over the leadership of the Department of Obstetrics and Gynecology. Immediately upon his arrival, he began to reorganize and modernize the medical and scientific approach of the maternity hospital. He was surprised by the difficulty of this task because of local political constraints and sometimes-virulent protests by the MLF (women’s liberation movement), particularly regarding the management of abortion. Despite all these obstacles, he successfully led the maternity hospital for 12 years with the help of professors François Béguin and Felix Krauer, and he organized and actively supported the development of links between the clinic and basic research with Professor Paul Bischof.

During this period, we were privileged to enjoy a high-quality education that prepared us for the practice of our specialty devoted to women’s health. Walter Herrmann’s insatiable intellectual curiosity and scientific rigor, as well as his approach to ethics-related issues, were a model for most of us.

At his departure from the University of Geneva, the first undersigned opened a private practice together with Professor Walter Herrmann and was privileged to benefit from his vast experience. He was a doctor unanimously appreciated by his patients for his clinical approach and his exceptional listening quality.

After his retirement, he chose to live in Grindelwald with his wife Nicole. He was passionate by the observation of animals and nature, and fed with great pleasure deer and birds that came close to his chalet. As a versatile artist, he expressed himself through painting, sculpture and striking collages that were sometimes provocative.
We were many to visit him to share our opinions about the changes within our specialty and listen to the wisdom of his advice.

Seriously affected in his health since one year, he never gave up, tirelessly supported by his wife, who accompanied him until his last moments.

We will miss his intellectual acuity and warm-hearted humor. But we are conscious, as many other friends to have had the privilege and honor to share the friendship of this man and this outstanding physician.

We convey our deepest sympathy to his wife Nicole, his children and grandchildren in the USA.

Dr. Claudine Bach Brioschi
Dr. Evellyn Floris
Translation Professor Paul Bischof

BIRTH ANNOUNCEMENTS

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

Morgan Talia Doherty – 6 pounds, 12 ounces
August 19, 2012 (Michelle Doherty and Leo Doherty, MD)

Alem Gebrewold – 7 pounds, 6 ounces
October 25, 2012 (AeuMuro Lake, MD and Taye Gebrewold)

Clara Yvette Martinez – 7 pounds, 9 ounces
December 10, 2012 (Alexandra McPencow, MD and Ludovic Blas Pierre Martinez)

Joseph Varughese Raju – 5 pounds, 12 ounces
December 17, 2012 (Joyce Varughese-Raju, MD and Robin Raju)

Angelina Loren Dulay Tiongco – 6 pounds, 6 ounces
December 21, 2012 (Antonette Dulay, MD and Alvin Tiongco)
GRANTS AWARDED

Dr. Hugh Taylor – NIH/NICHD – “Environmental Estrogen Induced Epigenetic Alteration of Uterine Stem Cells”

Ms. Caroline Albert (mentor Dr. Vikki M. Abrahams) – Lupus Foundation of America – “Can Hydroxychloroquine Prevent Adverse Pregnancy in Women with APS?”

Dr. Vikki M. Abrahams – March of Dimes – “Understanding, Predicting and Preventing Adverse Pregnancy Outcomes in Women with Antiphospholipid Antibodies”

Dr. Emre Seli – Thomas Jefferson University Subaward NIH Funded – “The Anti-Inflammatory mRNA-Binding Protein ZFP36 in Obesity and Metabolism”

Dr. Gil Mor – NIH/NICHD – Discovery to Cure Summer Program

Ms. Abiola Ayanfalu (mentor Dr. Sabrina Diano) – American Diabetes Association – Undergraduate Internship

Dr. Amanda Kallen (mentor Dr. Yingqun Huang) – Bennack-Polan Foundation – “H19 IncRNA-Mediated Regulation of Gene Expression in Granulosa Cells”

Dr. Heather Lipkind – HealthPartners Institute for Education and Research Subaward CDC Funded – Vaccine Safety Datalink Project

Dr. Gregory Gressel (mentor Dr. Aileen Gariepy) – ACOG – “Patient and Provider Perspectives on Bedsider.org in a Low Income, Racially Diverse Clinic Population”

Dr. Urania Magriples – Ministry of Health, Rwanda – “Building Human Resources for Health: Yale University and the Ministry of Health of Rwanda”

Dr. Elisabeth Erekson – NIH/NIA GEMSSTAR – “Vulvovaginal Skin Symptoms in Postmenopausal Women”

Dr. Elisabeth Erekson – Claude D. Pepper Older Americans Independence Center Career Development Award

Dr. Clare Flannery – NIH/NICHD – “Effect of Insulin on Estrogen Receptor Alpha Activity in Human Endometrial Cells”

Ms. Lisa An (mentor Dr. Nancy Stanwood) – Society for Family Planning – Trainee Research Award 2012

Dr. Xiao Xu – University of Michigan Subaward Blue Cross Blue Shield of Michigan Funded – “Women’s Utilization of Preventative Health Services”

Albert McKern Memorial Funds Recipients 2012:

Dr. Christina Han – “Elevated Risk of Preeclampsia in Diabetic Pregnancies: Elucidating Molecular Mechanisms, Effects of Therapies, and Novel Biomarkers”
Dr. Jessica Illuzzi – “Placenta Accreta in the 21st Century”

Paul Titus Fellowship Recipient 2012:

Dr Seth Guller – “Placental Microparticles and Endothelial Function in Preeclampsia”

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 (92.1)
- Yale Maternal-Fetal Medicine (89.7)
- Yale Reproductive Endocrinology (87.5)
- Yale Urogynecology (89.3)

YALE OB/GYN PHYSICIANS ON 2012 TOP DOCS LISTS

Physicians were selected based on a peer nomination process.

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

- Joshua A. Copel, MD (MFM)
- Michael J. Paidas, MD (MFM)
- Urania Magriples, MD (MFM)
- Pasquale Patrizio, MD, MBE (REI)
- Hugh S. Taylor, MD (REI)
- Alessandro D. Santin, MD (Gyn Oncology)
- Peter E. Schwartz, MD (Gyn Oncology)
- Masoud Azodi, MD (Gyn Oncology)
- Thomas J. Rutherford, MD, Ph.D. (Gyn Oncology)

(Dr. Charles Lockwood also made the list. He is no longer with Yale.)

Closer to home, Connecticut Magazine recognized four as “Top Doctors” in their 2012 annual survey:

- Michael R. Berman, MD (County Ob/Gyn Group PC)
- Ian M. Cohen, MD (Associated Women’s Health Specialists PC)
- Norman A. Ravski, MD (County Ob/Gyn Group PC)
- Howard Simon, MD (County Ob/Gyn Group PC)

(Drs. Charles Lockwood and Edmund Funai also made the list. They are no longer with Yale.)
U.S. NEWS & WORLD REPORT NAMES YNHH ONE OF THE NATION’S TOP HOSPITALS

Yale-New Haven Hospital has been included among the top hospitals in the United States, according to U.S. News & World Report’s annual “America’s Best Hospitals” issue.

YNHH is the primary teaching hospital of Yale School of Medicine. Gynecology services at Yale-New Haven were ranked 13th by U.S. News & World Report.

Best Nationally Ranked Hospital
Best Ranked #1 in Connecticut

Twelve Ob/Gyn doctors were selected based on a peer nomination process:

- Masoud Azodi, MD* (Yale Department of Obstetrics, Gynecology and Reproductive Sciences, Gyn Oncology)
- Joshua A. Copel, MD* (Yale Department of Obstetrics, Gynecology and Reproductive Sciences, MFM)
- Emily Fine, MD (Gynecology Group)
- Marsha K. Guess, MSc, MD (Yale Department of Obstetrics, Gynecology and Reproductive Sciences, Gyn Urology)
- Vincent Lynch, MD (Greater New Haven Ob-Gyn Group PC)
- Urania Magriples, MD (Yale Department of Obstetrics, Gynecology and Reproductive Sciences, MFM)
- Michael J. Paidas, MD* (Yale Department of Obstetrics, Gynecology and Reproductive Sciences, MFM)
- Pasquale Patrizio, MD, MBE* (Yale Department of Obstetrics, Gynecology and Reproductive Sciences, REI)
- Thomas J. Rutherford, MD, PhD* (Yale Department of Obstetrics, Gynecology and Reproductive Sciences, Gyn Oncology)
- Alessandro D. Santin, MD* (Yale Department of Obstetrics, Gynecology and Reproductive Sciences, Gyn Oncology)
- Peter E. Schwartz, MD* (Yale Department of Obstetrics, Gynecology and Reproductive Sciences, Gyn Oncology)
- Hugh S. Taylor, MD (Yale Department of Obstetrics, Gynecology and Reproductive Sciences, REI) (Dr. Charles Lockwood also made the list. He is no longer with Yale.)

* Denotes that a doctor, in Castle Connolly’s estimation, is among the top 1% in the nation in his or her specialty. Doctors listed in U.S. News “Top Doctors” without this indication are determined to be in the top 10% in their region.

NOTE: Doctors are listed in alphabetical order, and the results are not reflective of any rank order.
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
Siobhan Dolan, MD
Michael Kelly, MD
Annette LaMorte, MD
Orlando J. Miller, MD
Myron Nobil, 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?

President Richard C. Levin steps down from his position as President of the University at the end of the 2012-2013 academic year, his 20th year of service. He plans to take a year’s sabbatical leave, during which he hopes to write a book reflecting on both higher education and economic policy.

Peter Salovey, currently Yale’s Provost and the Chris Argyris Professor of Psychology, has been named as the University’s 23rd President. His appointment is effective June 30, 2013. He succeeds Richard C. Levin, who assumed the Yale presidency in 1993.

Hugh S. Taylor, MD, has been named the Anita O’Keeffe Young Professor and Chair of the Department of Obstetrics, Gynecology and Reproductive Sciences at Yale School of Medicine (YSM) and Chief of Obstetrics and Gynecology at Yale-New Haven Hospital (YNHH), effective October 1, 2012.

Cynthia Sparer has been promoted to Senior Vice-President of Yale-New Haven Hospital.

Peter E. Schwartz, MD, was honored with the prestigious Yale Cancer Center Lifetime Achievement Award at the fourth annual Yale Cancer Center Conclave on November 20, 2012. This award recognizes his innumerable contributions to the treatment of gynecologic cancers as well as his devoted service to Yale. Dr. Schwartz has provided over 40 years of dedicated service to our Department, students and patients.
**Gil Mor, MD, PhD**, will lead the new Division of Reproductive Sciences in the Obstetrics, Gynecology and Reproductive Sciences Department. Dr. Mor received his PhD from Weizmann Institute of Science and his MD and MSc from Hebrew University. He will also serve as the Director of the Yale Women’s Reproductive Health Research (WRHR) Career Development Program.

**Emre Seli, MD**, will be the new Director of the Division of Reproductive Endocrinology and Infertility and Chief of Reproductive Endocrinology and Infertility at Yale-New Haven Hospital. In his new role, Dr. Seli will be leading the Division’s clinical, research and educational programs.

**Lubna Pal, MBBS, MRCOG, MS**, will serve as the Associate Chair for Education in the Obstetrics, Gynecology and Reproductive Sciences Department. In this role, Dr. Pal will be overseeing all of the clinical training programs in the Department. She will work with Dr. Illuzzi (Medical Education Director) and Dr. Shaw (Residency Director) as well as each of the fellowship directors to coordinate and expand our already excellent Ob/Gyn educational program.

**Sabrina Diano, PhD**, will serve as the Associate Chair for Faculty Development. In this role, Dr. Diano will serve as a mentor to our research faculty, advising on career and program development. She, along with the clinical section chiefs, will also be available to provide research career mentoring for the clinical faculty.

**Catalin Buhimschi, MD**, has been appointed Maternal-Fetal Medicine Section Chief and Vice-Chair of the Department of Obstetrics and Gynecology at Ohio State University. He will begin his new position on April 1, 2013.

**Irina Buhimschi, MD**, has been appointed Director of the Center for Perinatal Research in The Research Institute at Nationwide Children’s Hospital in Columbus, Ohio. She will begin her new position on April 1, 2013.

**Michael Paidas, MD**, will assume the role of Interim Section Chief, Maternal-Fetal Medicine Division in the Obstetrics, Gynecology and Reproductive Sciences Department.

**Elisabeth A. Erekson, MD**, has accepted a position at Dartmouth-Hitchcock Medical Center, Manchester, New Hampshire.

**Se-Te Joseph Huang, MD**, has accepted a position at The Ohio State University College of Medicine, Columbus, Ohio.

**Pasquale Patrizio, MD**, served as a Co-Chair of the postgraduate course “Regenerative Medicine: Promise, Pitfalls and Realities” at the ASRM 2012 Annual Scientific Meeting.

**Mark Silvestri, MD, and Antonio Maldonado, MD**, were both elected as Administrative Chief Residents for the 2012-2013 academic year.

**Fundraising:** The Maternal-Fetal Medicine Preemie-Donnas annual fundraiser in support of the March of Dimes for Babies received over $2,200 this year. The Maternal-Fetal Medicine fundraiser for the March of Dimes at Geronimo’s in New Haven sold $389 in raffle tickets. The raffle winner, **Sarah Cross, MD**, donated it back to the March of Dimes.

Discover to Cure has received over $56,000 this year; over $19,000 was raised from the Fifth Annual Discovery to Cure Walk to benefit ovarian cancer research, which was held at Sherwood Island State Park in Westport, Connecticut, on September 16, 2012.
YNHH announced the completion of its acquisition of the Hospital of Saint Raphael. On September 11, 2012, officials from Yale-New Haven Hospital and the Hospital of Saint Raphael signed the final documents. The acquisition will provide many benefits, including greater overall efficiency and economies of scale, increased physician alignment, integration of the electronic health record and, with the addition of 511 beds, increased capacity for Yale-New Haven Hospital. With the combined highly skilled physicians and staff, Yale-New Haven is one of the largest hospitals in the country, with over 1,500 beds.

YNHH OB Council News: Lactation Services team leaders are Heather Lipkind, MD, and Katie Agis. Cesarean Section Efficiency team leaders are Joel Silidker, MD, and Katie Donohue. Induction Flow and Efficiency team leaders are Steven Fleischman, MD, and Caroline Joseph-Keegan. Patient Education team leaders are Shefali Pathy, MD, Tracy Savage and Richard Jennings.

The YNHH Gynecology Operations Council has been established. It is a multidisciplinary group whose purpose is to help direct efforts to provide patients with the best care possible and make YNHH the hospital of choice for gynecologic care. The co-chairs are Linda Fan, MD, and David Lima, MD.

FACULTY PROMOTIONS EFFECTIVE JULY 1, 2012

Sabrina Diano, PhD, to rank of Professor in the Traditional Track with tenure

Anna Sfakianaki, MD, to rank of Associate Professor – CE Track

RESEARCHER PROMOTIONS EFFECTIVE JULY 1, 2012

Ayesha Alvero, MD, to rank of Research Scientist

VOLUNTARY FACULTY PROMOTIONS EFFECTIVE JULY 1, 2012

Steven Fleischman, MD, to rank of Associate Clinical Professor
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

Joy J. Carrigan
Yale School of Medicine
Office of Development
203-436-8541
Joy.carrigan@yale.edu
NETCASTS AVAILABLE ON ITUNES

Next time you’re downloading your favorite music from iTunes, don’t forget to add a few Yale netcasts to your playlist. The number of downloadable files available is continuously increasing, thanks to the Office of Public Affairs. The netcasts include talks by alumni, faculty and other Yale-affiliated speakers. All netcasts are free from iTunes, so download them now at http://opa.yale.edu/netcasts.aspx.

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

YFC: http://www.facebook.com/pages/Yale-Fertility-Center/55523238825?ref=ts


Yale Program for Menopause: http://www.facebook.com/pages/Yale-Menopause-Program/77498424812

Yale Program for In vitro Fertilization: http://www.facebook.com/pages/Yale-In-Vitro-Fertilization-Program/88633862352


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

Name: __________________________  Year: __________________________

Street: __________________________  City: __________________________

State: __________________________  Zip: __________________________  Country: __________________________

☐ Check if this is a new address

Tel: __________________________  Fax: __________________________  Email: __________________________

Tell us your news (marriage, birth, death, career milestones, honors, etc.):

________________________________________________________________________________________

________________________________________________________________________________________

If you are advising us of an alumni death, please provide us with the following:

Name of deceased: __________________________

Class year: __________________________

Approximate date of death: __________________________

Contact name and phone number: __________________________

Does the family of the deceased wish to continue receiving mail from YOGS? ☐ Yes ☐ No

Please email completed form to: yogs@yale.edu or fax to 203-737-1883. Or mail to:

Yale University School of Medicine
Department of Obstetrics, Gynecology and Reproductive Sciences
333 Cedar Street, PO Box 208063, FMB 337
New Haven, CT 06520-8063
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.

Retain this portion for your records

YOUGS MEMBERSHIP INVOICE

Name (Last)    (First)    (Middle Initial)         (Degree)
Institution/Practice Name
Street Address      Office/Suite #
City   State/Province             Zip/Postal Code  Country
Phone (_____) ______________________________    Email Address ______________________________
Spouse/Partner’s Name ___________________________________________________________________

Membership Dues (please check one)
☐ One Year      $150      ☐ Two Years      $200
☐ Lifetime Membership     $1,500

Two ways to pay:
2. By Check Payable to Yale Obstetrical and Gynecological Society (YOGS):
   Mail to:
   Yale University School of Medicine
   Department of Obstetrics, Gynecology and Reproductive Sciences
   333 Cedar Street, FMB 337
   PO Box 208063
   New Haven, CT 06520-8063
   Attn: Dianna Malvey