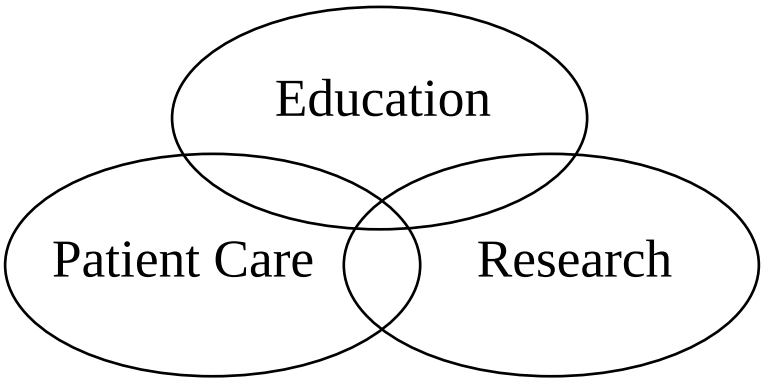
University of Washington

Department of Obstetrics and Gynecology

2010–2011
Resident Applicant Information



UW Medicine
SCHOOL OF MEDICINE

Administration

Established in 1948, the Department of Obstetrics and Gynecology has a faculty of 41 physicians, four PhD basic scientists, nine fellows, four nurse practitioners and five certified nurse-midwives, with 24 residents in training.

David A Eschenbach, MD, has served as the department Chair since June 2002. Of the 17 faculty members for whom subspecialty certification is available, 15 are board certified in their subspecialty and the other two are active candidates. All our faculty are board certified in Ob/Gyn except six junior faculty who are active candidates.

Administration

Chairman:	David Eschenbach, MD	
Vice Chairs:	Thomas Benedetti, MD, MHA	
	Michael Gravett, MD	
Administrative Director:	Farel McClure, MA	(206) 543-0929
Assistant to the Chair:	Ellen Corke	(206) 616-8305
Residency Program Director:	Seine Chiang, MD	(206) 543-9626
Residency Program Coordinator:	Elizabeth Jarrett	(206) 543-9626

Department

Phone:	(206) 616-8305
Fax:	(206) 543-3915
Office of the Chair:	(206) 616-8305
Mailing Address:	University of Washington Department of Obstetrics and Gynecology Box 356460 Seattle, WA 98195-6460

Divisions

Education:	Thomas Benedetti, MD, MHA	(206) 543-3891
Gynecologic Oncology:	Barbara Goff, MD	(206) 685-2463
Maternal-Fetal Medicine:	Michael Gravett, MD	(206) 543-3729
Reproductive Endocrinology & Infertility:	Currently Open	
Urogynecology:	Gretchen Lentz, MD	(206) 543-5555
UWMC Women's Health:	Seine Chiang, MD	(206) 543-9626
HMC Women's Health:	Susan Reed, MD, MPH	(206) 744-8563

EDUCATION

EDUCATION Division

The Education Division has responsibility for coordinating faculty development programs, Grand Rounds, Continuing Medical Education (CME) programs in Women's Health, and undergraduate and graduate medical education in obstetrics and gynecology. This division provides oversight for the development, implementation and consistent application of curriculum objectives and follows the national guidelines (Undergraduate—APGO, UMEC; Graduate—CREOG, RRC, ACGME).

Residency Leadership

Seine Chiang, MD
Assoc Prof, Women's Health
Residency Program Director
Division Dir, Women's Health

Zane A Brown, MD
Prof, Maternal-Fetal Medicine
Assoc Residency Prgrm Director

Michael F Fialkow, MD, MPH
Asst Prof, Urogynecology
Dir, Resident Surgical Skills Curric

Medical Student Leadership

Thomas J Benedetti, MD, MHA
Professor, Maternal-Fetal Med
Education Division Director

Vicki Mendiratta, MD
Assoc Prof, Women's Health
Ob/Gyn Clerkship Director

Clinician Educators

Rebecca Dunsmoor-Su, MD, MSCE
Asst Prof, Women's Health
Residency Research Advisor

Anne-Marie Amies Oelschlager, MD
Asst Professor, Women's Health
Pediatric/Adolescent Gyn Education

Ron E Swensen, MD
Associate Professor, Gyn Onc
Gyn Onc Education

Gretchen M Lentz, MD
Associate Professor and
Division Director, Urogynecology
Urogynecology Education

Brenda Houmard, MD, PhD
Assistant Professor, REI
Reproductive Endocrinology
and Infertility Education

Sarah W Prager, MD, MAS
Asst Professor, Women's Health
Family Planning Education

Kirkwood K Shy, MD, MPH
Professor, Women's Health
Gynecology Education

Clinical faculty who work with our residents as liaisons to the Education Division:

- William Peters, MD, and Elise Everett, MD—Swedish Gynecology/Oncology
- David Luthy, MD, and Brigit Brock, MD—Swedish Obstetrics
- Linda Mihalov, MD—Virginia Mason Gynecology
- Roger Rowles, MD—Yakima Valley Memorial Hospital
- Tracey Flum, MD—Group Health Central

Education and Training

RESIDENCY PROGRAM

Message from the Residency Program Director

"The goal of our residency training program is to provide a balanced clinical experience with individualized teaching by nationally recognized experts in the field, complimented by formal education activities such as didactics, journal club, and a nationally renowned surgical skills curriculum and simulation. A long-standing partnership between the University of Washington Medical Center and carefully selected affiliate hospitals provide our residents with a unique blend of ethnically diverse patients, different clinical settings, and extensive surgical and ambulatory care experiences. The true strength of our residency program, however, lies in the residents themselves—culturally sensitive, caring, bright, inquisitive young people!"

Residency Program Director
Associate Professor, Department of Obstetrics and Gynecology
Division Director, Women's Health
Associate Medical Director, Roosevelt Women's Health Center

University of Washington Obstetrics and Gynecology Residency Training Program

- Fully accredited by the ACGME (2007) for 6 categorical positions per year
- Residency teaching provided by a dedicated team of University and community faculty:
  - 45 clinical faculty at UWMC and Harborview Medical Center (HMC)
  - 4 fellows in Gynecologic Oncology plus 5 fellows in Maternal-Fetal Medicine
  - Volunteer teaching faculty at Swedish Gynecologic Oncology group *(6 gynecologic oncologists)*, Swedish Perinatal Medicine group *(9 perinatal specialists)*, Virginia Mason *(3 gynecologists and 2 gynecologic oncologists)*, Pacific Northwest Fertility *(3 REIs)*, Yakima Valley Memorial *(3 obstetrician/gynecologists)*, and Group Health Central *(8 perinatal specialists).*

Educational Innovations

- Introduction of a comprehensive one-wk PGY1 orientation, including hands on training in basic OB skills, common office procedures, and Gyn surgical skills utilizing dry lab simulation and porcine lab
- Introduction of OB simulation drills for routine OB procedures *(operative vaginal deliveries)* and OB emergencies *(eclampsia, hemorrhage, shoulder dystocia)*
- Designation as one of the ACOG-approved sites for future national simulation testing and also one of 14 residency training programs nationally designated by Intuitive Surgical for da Vinci Robotic surgical training for Ob/Gyn residents and Gyn Onc fellows
- Disclosure training project using actors aimed at teaching our residents to effectively and ethically disclose medical errors
- Continuation of our rigorous surgical skills curriculum and our nationally-recognized simulation center (ISIS)

Education and Training

RESIDENCY PROGRAM

Residency Application Process

Over 500 completed residency applications are reviewed annually, with the selection committee granting approximately 70 interviews for six first-year resident positions.

> Interviews are offered as completed files are reviewed. Therefore, **EARLY** submission and completion of applications is **key**. No application will be accepted after **October 1st,** although interview slots may be filled prior to this date.

An applicants file is considered complete when we have received the following documents:

— ERAS common application *(which includes the CV)*
— Personal statement
— USMLE or COMLEX scores
— Medical school transcripts
— 1 letter of recommendation *(preferably by an Ob/Gyn) (3 total by November 1st)*

Applicant interviews are conducted during late October and the months of November and December. The selection committee consists of eight interviewers: the department chair, residency program director, associate residency program director, faculty representatives from the various divisions, patient-centered care committee, and a team of two residents.

Housestaff Salary

All prospective residents must provide written confirmation that they were informed of the University of Washington Graduate Medical Education Residency Position Appointment and Policy, which outlines the terms of agreement during their residency training at the UW.
All applicants are informed that this is available on our GME website:
http://www.uwmedicine.org/Education/ResidenciesAndFellowships/
Click on "Incoming Residents & Fellows" on the menu.

Approved Housestaff Compensation Rates July 1, 2009

Level	*Annual Salary*	*Monthly Rate*
R1	$47,341	$3,945
R2	$49,248	$4,104
R3	$51,036	$4,253
R4	$52,944	$4,412

Housestaff Benefits

Housestaff benefits include:

— Medical and dental insurance
— Stipend for on-call meals on most rotations
— On-call sleep rooms
— Physician lab coats
— Annual vacation of 3 weeks *(5 weekdays and 2 weekend days constitute one week)*
— UW retirement plan *(contributions up to 5% with 1:1 matching)*

University of Washington

Department of Obstetrics and Gynecology Residents 2010–2011

R4


Laura A Cieslik, MD
Univ of Southern California


Laura Jacques, MD
Univ of Wisconsin, Madison


Joshua E Kilgore, MD
New York Medical College


Richelle N Medford, MD
University of Maryland


Anna R Shope, MD
University of Washington


Mary Beth Thake, MD
Southern Illinois University

R3


Karen L Bar-Joseph, MD
University of Washington


Corey M Eymard, MD
University of Virginia


Kara K Hoppe, DO
Chicago College of Osteopathic Medicine


Haider S Mahdi, MD
Kufa College of Medicine
Republic of Iraq


Sara A Thompson, MD
University of Washington


Andrea M Zins, MD
University of Minnesota

R2


Eric G Adiarte, MD
University of Minnesota


Anna L Altshuler, MD, MPH
University of California, Irvine


Dina M Gordon, MD
New Jersey Medical School


Meghan A McSorley, MD
PhD, MPH
University of Pittsburgh


Mary (Tilley) Jenkins Vogel, MD
University of North Carolina


Andrew E Warner, MD
University of Washington

R1


Emily J Amarosa, MD
Harvard Medical School


Dawn M Flandermeyer, MD, MPH
George Washington Univ


Joelle Lucas, MD
University of Washington


Timothy B Mitchell, MD
New York Medical College


Anna T Panighetti, MD
University of California, SF


Caroline E Rouse, MD
Indiana University

Education and Training

RESIDENCY PROGRAM

Synopsis of Clinical Experience

The Ob/Gyn Residency Review Committee (RRC) tracks specific procedures and primary care diagnoses through the ACGME's web-based caselog system (OPLOG). Below is a representative listing of the average number and type of cases that first through fourth year residents logged into the ACGME database as primary surgeon. As you can see, our residents have the opportunity to perform many major and minor gynecologic surgeries during their first year of training.

The cumulative data is a compilation of the 2010 data provided to us by the recent graduates in their roles as primary surgeon over the four years of training. These numbers represent average numbers per resident.

Average GYNECOLOGY Case Experience as Surgeon by Year of Training 2009–10

Level	*TAH*	*TVH*	*L-Hyst*	*UroGyn*	*Op LSC*	*Op HSC*	*Ab**	*USG*	*Ca*
R1	16	10	3	25	29	21	12	20	33
R2	16	0	7	6	22	13	11	115	57
R3	17	19	14	46	33	17	22	13	7
R4	40	11	15	67	36	23	12	3	74
Cumulative primary surgeon over all 4 years:									
'10 Grads	102	34	31	133	103	57	53	139	148

**Our department receives funding as part of the nationally recognized Ryan Training Program to enhance abortion and family planning education and services. Residents have the option to "opt out" of providing abortion services, but are expected to participate in family planning services & counseling.*

Average OBSTETRICS Case Experience as Surgeon by Year of Training 2009–10

Level	*Vaginal Delivery*	*Operative Delivery*	*Cesarean Delivery*
R1	130	8	26
R2	25	2	106
R3	56	11	73
R4	17	9	13
Cumulative primary surgeon over all 4 years:			
2010 Grads	241	31	230

Education and Training

RESIDENCY PROGRAM

Representative Rotation Schedule 2010–2011

R1	Swedish Gyn	UW OB	UW Gyn Onc	UW Night Float	GH OB/ UW Amb	GH OB/ UW Gyn	Yakima Ob/Gyn	UW Benign Gyn
R2	UW OB Antepartum and clinics	REI	HMC Gyn	UW OB Night Float	UW OB L&D & Postpartum		UW Gyn Onc	
R3	HMC Gyn	Swedish OB	UW OB Antepartum and clinics	VA/VM Gyn	HMC Ambulatory		Yakima Ob/Gyn	Elective
R4	Swedish Gyn	UW Urogynecology	UW Gyn Onc	UW OB	UW OB Night Float		UW Benign Gyn	

Swedish = Swedish Medical Center, First Hill
GH = Group Health Cooperative
HMC = Harborview Medical Center
Yakima = Yakima Valley Memorial Hospital
VA = Veteran's Administration, Puget Sound
VM = Virginia Mason Medical Center
UW = University of Washington Medical Center

OB Antepartum = High-risk obstetrics antepartum
OB Postpartum = Labor & Delivery day coverage
OB Night Float = Labor & Delivery night float
UW Amb = Women's Health

Total Time Spent by Level of Training in Each Major Clinical Area, 2009–10

Level	*Rotations*	*Time Spent*
R1	Obstetrics	20 wks
	Gynecology	14 wks
	Gynecologic Oncology	8 wks
	Ambulatory Women's Health	2 wks
	Rural Obstetrics and Gynecology *(Yakima)*	4 wks
R2	Obstetrics	24 wks
	Gynecology	8 wks
	Gynecologic Oncology	8 wks
	Reproductive Endocrinology and Infertility	8 wks
R3	Obstetrics	16 wks
	Gynecology	16 wks
	Primary Care and specialty clinic	8 wks
	Elective—Research or International Health	4 wks
	Rural Obstetrics and Gynecology *(Yakima)*	4 wks
R4	Obstetrics	16 wks
	Gynecology	16 wks
	Gynecologic Oncology	8 wks
	Urogynecology	8 wks
Total for All 4 Yrs	Obstetrics	76 wks
	Gynecology	54 wks
	Gynecologic Oncology	24 wks
	Urogynecology	8 wks
	Reproductive Endocrinology and Infertility	8 wks
	Primary Care and specialty clinics	8 wks
	Ambulatory Women's Health	2 wks
	Elective—Research or International Health	4 wks
	Rural Obstetrics and Gynecology	8 wks

Education and Training

CLINICAL TRAINING SITES

University of Washington Medical Center (UWMC) is the primary institution for residency training. It is a 450-bed teaching and research hospital that offers comprehensive medical care, including complete medical, surgical, obstetric, gynecologic and psychiatric services. In addition, there is a Neonatal Intensive Care Center, a Primary Care Center, and a unique Institute for Simulation and Interprofessional Studies (ISIS). The Medical Center has joined with the Fred Hutchinson Cancer Research Center and Seattle Children's to create the Seattle Cancer Care Alliance (SCCA), an integrated ambulatory and inpatient cancer care center. UWMC offers residents a wide mix of inpatient and ambulatory patients from primary care to specialized tertiary care. UWMC also offers abundant opportunities to conduct research.

The Obstetrical Unit at UWMC is a referral center for a large geographic region ranging from Alaska to Montana, that includes most of the State of Washington and serves a large number of high-risk deliveries and high acuity antepartum patients. Approximately half of the 2200 annual deliveries at UWMC are direct hospital-to-hospital high-risk transfers and patients cared for in UW maternal-fetal medicine subspecialty clinics. In the Obstetrical Unit, residents are the center of the care model and provide direct care for a wide variety of medically complicated pregnancies. Milliman & Robertson *(a national actuarial firm)*, rated the acuity of the service at 1.98, the highest they ever calculated.

The Gynecologic Oncology service at UWMC is extremely busy with over 850 diagnosed cancer patients per year. Residents operate at least three days per week on the service. Residents regularly are exposed to gynecologic malignancies, complicated pelvic surgeries, intensive care medicine, and perioperative complications due to patients with many co-morbid conditions. A four-year gynecologic oncology fellowship began in 2005; fellows rotate on the UWMC and Swedish Hospital Medical Center (SHMC) oncology services.

The Gynecology services at UWMC care for a wide variety of gynecologic conditions, with 1200 new patients seen in clinic per year. A busy surgery schedule of two days a week of inpatient and outpatient surgery, including urogynecology, exposes residents to a breadth of gynecologic procedures in a setting of high patient comorbidities. The 1st and 4th year residents on the Gynecology service and the 4th year on the Urogynecology service cross cover the UWMC Emergency Department and inpatient gynecology consultation requests. The Gynecology service residents also gain valuable ambulatory experience at the Roosevelt Women's Clinic where they provide routine and specialized gynecologic care. Specialty clinics, such as Vulvovaginitis Clinic and Dysplasia Clinic, add to their clinical experience.

As UWMC is primarily a tertiary care facility, rotations at SHMC, HMC, VMMC, GH, the VA and YVMH are valuable to provide different practice models with populations of broad ethnic diversity and an extensive range of obstetrical and gynecological experience. At all institutions, an attending physician is present for all surgeries and deliveries, and is available in all resident continuity clinics to supervise clinical care and provide teaching.

Education and Training

CLINICAL TRAINING SITES

Harborview Medical Center (HMC) is owned by King County and is managed by the University of Washington. Unique features of the Harborview Ob/Gyn resident rotations include exposure to management of obstetric trauma in a Level I trauma center, a nationally recognized program for the management of patients after sexual assault, and an ethnically and socially diverse population. Forty percent of patients are non-English speaking (with a large proportion from Africa and Asia), and trained interpreters are available for all such patient care. In addition, HMC has a Family Planning Clinic developed through the Kenneth Ryan Fellowship. This provides residents exposure to a depth and breadth of Family Planning services, including hormonal contraception, IUDs, medical and surgical terminations of pregnancy, which would not be available otherwise.

The gynecology rotations include inpatient and outpatient surgical care, and outpatient clinics. Residents on service at HMC cover emergency room call for obstetrical and gynecological trauma, gynecology emergency, and sexual assaults. In addition, the Ob/Gyn Department has a primary care rotation at HMC for one 3rd year Ob/Gyn resident, who is supervised by both internal medicine and our Ob/Gyn faculty. This rotation includes two primary care clinics, a Dermatology Clinic, a Breast Clinic, and an HIV Obstetric Clinic, providing residents with significant exposure to ambulatory primary care for women in a heterogeneous, multi-cultural, lower socio-economic population in a county hospital setting.

Virginia Mason Medical Center (VMMC) is a private, non-profit organization which has an affiliation teaching agreement with the University of Washington for residents and medical students. VMMC is a large, multi-disciplinary group practice and 307-bed hospital in downtown Seattle. The gynecology rotation provides the 3rd year resident with a broad and in-depth exposure to all aspects of operative gynecology, including endoscopy, gynecologic oncology, pelvic floor reconstruction, and infertility. Residents work closely with three experienced, board certified gynecologists and two gynecologic oncologists. This rotation gives residents experience with a different practice model, as well as extensive operative experience. The 3rd year resident serves as chief resident of the service.

Education and Training

CLINICAL TRAINING SITES

Swedish Medical Center (SMC), First Hill is a large, private hospital in downtown Seattle with a large gynecology service composed of both benign and oncology patients. SHMC has gynecologic oncologists who perform 270 cases per year and gynecologic surgeons who do 2800 major cases per year. SHMC does over 6000 deliveries annually and has a busy high-risk maternal-fetal medicine program. Both the obstetrical and gynecology services have full-time faculty with enthusiasm for and dedication to resident education. Their services round out the resident clinical experience and substantially increase their surgical experience.

The R1 and R4 on the Swedish gynecology rotation work with a specially designated teaching panel of dedicated gynecologic oncologists, general gynecologic surgeons, and reproductive endocrinology surgeons. An extensive operative experience is gained in complicated pelvic surgeries and benign disease, as well as basic vaginal, urogynecologic, and endoscopic gynecologic cases. These surgical cases fill the resident's operative schedule four to five days per week.

The R2 on the Reproductive Endocrinology rotation works closely in the clinic three days a week with three board certified reproductive endocrinologists (SHMC's Pacific Northwest Fertility group), evaluating patients with infertility and managing endocrinologic and congenital abnormalities. During this rotation, the resident performs endoscopic cases with Dr. Heath Miller, an expert in complicated laparoscopic surgery.

The R3 serves as the chief of the Swedish perinatal service, responsible for the management of high-risk antepartum patients, Cesarean and operative vaginal deliveries, and peripartum ICU patients. Additional training in performing and interpreting obstetrical ultrasound, both normal and abnormal, is provided.

Yakima Valley Memorial Hospital (YVMH) is a private, 223-bed, community-based hospital in Central Washington that serves a large rural area. First year residents on the Yakima rotation experience a community style of practice in an ambulatory setting where supervising Ob/Gyn attendings provide primary, obstetrical and gynecologic care for their patients. Residents at Yakima Valley Memorial also perform deliveries on patients to broaden their exposure to low-risk obstetrics.

Education and Training

CLINICAL TRAINING SITES

Group Health Central (GH) is a private hospital in an urban setting which offers a system of integrated health services, including extended educational opportunities for our first-year residents in low-risk obstetrics. Residents spend 2 days/week, 24-hour in-house OB call at Group Health Central, averaging 35 deliveries per month.

VA Puget Sound Health Care System is the largest referral medical center (504 total beds) in the Northwest Network and is part of the Veterans Integrated Service Network (VISN) 20, which includes facilities in Anchorage, Boise, Portland, Roseburg, Spokane, Seattle/Tacoma, Walla Walla and White City. In the past year, the VA Puget Sound had out-patient visits and more than 8,318 inpatient treatments for close to 60,000 unique patients. At this site, the 3rd year Ob/Gyn resident learns to serve as a consultant (evaluating, formulating a plan, and communicating with the referring provider), determine when a patient needs surgical intervention, optimize peri-operative management, perform various in-office procedures, and understand the unique psychosocial components of caring for women veterans.

.

Education and Training

GLOBAL HEALTH

Women's Health International Program (WHIP)

The goal of the University of Washington Department of Obstetrics & Gynecology **Women's Health International Program (WHIP)** is to improve women's health worldwide by providing health education for women, training for their health care providers, and by conducting research on key questions in women's health.

Resident Global Health Experience

Since 2003, over half of our residents have traveled to other countries for elective rotations. Residents are matched with a faculty mentor who oversees preparation for the rotation, including targeted reading in key areas of infectious diseases, obstetric emergencies and neonatal evaluation. In-country supervisors ensure that the resident experience meets ACGME educational objectives. The global health elective is four weeks long.

UW Ob/Gyn Global Health Webpages

http://www.obgyn.uwmedicine.org *(select Global Health from the category list in the upper left)*

Elective Sites

Lima, Peru

La Maternidad, the National Institute for Maternal and Perinatal Care, was established 182 years ago and has the highest designation awarded by the Health Ministry. They have eight ventilators for >17,000 deliveries/year.

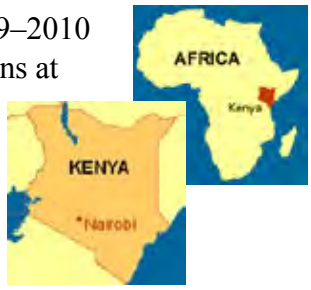
Hospital San Juan de Lurigancho, one of the smaller hospitals on the outskirts of Lima, is located in the District of San Juan de Lurigancho, which is one of the districts of Lima, Peru, and the most populous with over 1 million inhabitants. It was founded in 1976, initially in the capacity of a local health clinic. In 2005, it was upgraded to a level II-1 hospital. This designation indicates that the hospital is able to provide services in four major areas: Internal Medicine (outpatient and inpatient), Gynecology and Obstetrics, Surgical Services, and Pediatrics, Total capacity is 75 beds, and they are the main hospital for a population of ~1 million. They have two fetal monitors but no ventilators. Their goal is to become a level II-2 hospital, which involves expanding services they provide.

Education and Training

GLOBAL HEALTH

Nairobi, Kenya

Kenyatta National Hospital in Nairobi is under development for the 2009–2010 academic year. Three alumni of the residency program did elective rotations at Kenyatta in years past, primarily working on a variety of research projects focusing on HIV-1 infection in women. The new rotation will be clinically focused, similar to Lima, but will also provide exposure to the large community of infectious disease researchers based in Nairobi.



Kenyatta National Hospital is the University of Nairobi teaching hospital and is the largest hospital in Kenya. Maternal mortality has been reported to be as high as 1000 per 100,000 live births, and breast and cervical cancer are the leading causes of cancer death in women. Kenyatta provides comprehensive obstetric and gynecologic care for referral patients from all over Kenya, and provides a rich clinical learning opportunity.

Ob/Gyn Faculty Working Internationally

Our faclty participate in research and policy initiatives in India, Peru, Kenya, and Ethiopia. In collauboration with the School of Public Health and the Department of Global Health, this involvement is growing rapidly.

Current faculty participation:

• Anne-Marie Amies Oelschlager, MD	Ethiopia
• Thomas R Easterling, MD	India, South Africa
• Linda O Eckert, MD	Kenya, Worldwide
• Michael G Gravett, MD	Worldwide
• Benjamin E Greer, MD	China
• Jane E Hitti, MD, MPH	Kenya
• Connie Mao, MD	Ethiopia
• Caroline M Mitchell, MD, MPH	Ethiopia, Peru
• Sarah W Prager, MD, MAS	Zambia, Uganda, Nepal
• Jennifer A Unger, MD, MPH	Kenya
• Dilys M Walker, MD	Mexico

Education and Training

RESIDENCY PROGRAM

Resident Elective/Research Overview

One of the Residency Program's educational objectives is to provide an opportunity for the residents to conduct original research. During the R3 and R4 years, including use of the allotted R3 elective time, residents must conduct their research, gather and analyze their data, and prepare a presentation for Resident Research Day, where R4s present their research to the department and Ob/Gyn community. The research/elective experience is designed to create a pathway to foster reading and the analysis of medical literature in the years following residency.

Past 4 Years of R3 4-week Elective Sites/Study

Resident	***Location***	***Area of Elective Study***
Class of 2011		
Cieslik	Seattle	Research at Pacific Northwest Fertility
Jacques	Seattle	Robotics training and certification; maternity leave
Kilgore	Texas	MD Anderson Gyn Onc elective, patient care and didactics
Medford	Lima, Peru	Providing care to women
Shope	Nairobi, Kenya	Providing care to women
Thake	Seattle	Minimally invasive surgery at Swedish (robotics certified) & research
Class of 2010		
Carranza	Lima, Peru	Providing care to women, researching factors affecting maternal mortality
Lewis	Lima, Peru	Providing care, understanding maternal health, morbidity, mortality
McLean	Seattle	Ovarian cancer in elderly, pelvic exenteration in modern chemoradiation
McLemore	Lima, Peru	Providing care to women
Tenpenny	Yakima	Rural medicine
Thomas	Seattle	Home births/transfers; Lead Follicle Project
Class of 2009		
Debiec	Nicaragua	Providing healthcare for women in rural Nicaragua
DeSano	Nepal	Medical care to underserved people in remote regions of Himalayas
Lee	Nicaragua	Primary Ob/Gyn care for women in rural Nicaragua
Lorentz	Nicaragua	Primary Ob/Gyn care for women in rural Nicaragua
Chang	Seattle	Operative and clinical experience; transition to UW residency
Sementi	Seattle	Operative and clinical experience; ACOG conference; research project
Class of 2008		
Nathan	Nicaragua	International volunteer medical missions
Norquist	NYC Sloan-Kettering	Galloway Fellowship in Gynecologic Oncology
Simmons	STD Clinic in Peru	Colposcopy in female sex workers; medical Spanish class
Norland	Nairobi, Kenya	Ob/Gyn experience in Nairobi; research to improve healthcare for women in the Third World
Stephenson-Famy	India	Assessing burden of malaria in pregnancy in India
Marrs	Costa Rica/Guatamala/ Nicaragua	Clinical work and Spanish language immersion

Education and Training

RESIDENCY PROGRAM

2010-11 Required Department Educational Activities

All Ob/Gyn residents listed are required to attend these activities, unless they have obtained special permission to be excused. Each division is responsible for providing clinical service coverage.

Day	***Activity***	***Required***
Aug 4, 2010	Annual Resident Retreat	Each division is responsible for its own attending coverage until 5:00 pm. Location—Waterfront Activities Center after Grand Rounds
September 1 annually	ABOG Application	Chief Residents: Time to register with ABOG and apply for ABOG exam, scheduled for the last Monday in June. www.abog.org
November 15 annually	ABOG Exam Final Registration	Chief Residents: Application for June exams must be finalized, along with your exam fee—NO exceptions! www.abog.org
As scheduled	Surgery Labs	Dry Labs and Porcine Labs
January annually	Resident Research Day Applications Due	R2 residents submit their research application
Jan 21, 2011	CREOG In-Service Exams	Residents will take exam in shifts. Details TBA.
Feb 9, 2011	Legislative Day	Residents as scheduled; not all will attend. Details TBA. 8:00 am – 2:30 pm
Feb 18, 2011	Res Rsch Day Absts Due	
Feb 16, 2011	Ski Day	8:00 am to 5:00 pm, Snoqualmie Pass
Mar 23, 2011	Resident Research Day	7:30 am to 1:00 PM, South Campus Center *(tentative date)*
June 2011	Resident Roast	Date and time TBA
June 15, 2011	NRP Training	
June 18, 2011	Senior Resident & Fellow Graduation Banquet.	Sand Point Country Club, 6:00 pm
June 27, 2011	ABOG Exams	All Chiefs at testing centers. R4 level residents must have applied to ABOG before November 15th of prior year.

Other Resident Requirements and Department Activities of Note

Grand Rounds—Wednesday mornings, 8:00 am to 9:00 am, September through May	As listed on Grand Rounds Schedule online at http://www.obgyn.uwmedicine.org *(click on Department Calendar & News)*
Resident Didactics/Lectures/Conferences *(required):* • Morbidity and Mortality Conference @ 9:00 am • Didactics 10:00 am to 12:00 pm • Presurgery conference @ 12:00 pm	Wednesday mornings 9:00 am to noon in BB-667
QI Conferences	Quarterly
Faculty Research Hour	10:00 am 1st Wed of the month during the school year
Journal Club—Wednesday evenings at 7:00 pm	6 times/year at faculty homes
Resident Evaluation Committee	November and May annually, 9:00 am to noon
Faculty Meetings	Monthly—4th Wednesday of the month at 7:00 am
Faculty Development Workshop	Annually in September
Resident Applicant Interviews	Mondays 7:15 am to 1:30 pm Late October; November; December

Education and Training

RESIDENCY PROGRAM

Ob/Gyn Resident Surgical Simulation Education Curriculum

Program Overview

The foundation for the Surgical Education and Research Program (SERP) began in 1997 when Drs. Barbara Goff, Gretchen Lentz and Lynn Mandel began a series of studies modeled on work done in general surgery, showing that bench or inanimate trainers and live animal models can improve the surgical skills of untrained Ob/Gyn residents before they enter the operating room. Further studies here and around the country continue to demonstrate that repetitive practice of technical skills and simulation of virtually every aspect of procedural and technical skills improves performance. Around the same time, the University of Washington School of Medicine also foresaw this evolving paradigm shift in surgical education and began development of the Institute for Simulation and Interprofessional Studies (ISIS), where simulation performance could be measured, validated, and perfected in a controlled and safe environment. The validated curricula for Ob/Gyn training will be fully developed by combining our prior experience training Ob/Gyn residents with their multidisciplinary faculty experts. Because the curricula are designed to capture data on performance and to immediately provide feedback, residents will train in a safe environment to reduce or eliminate errors.

Michael F Fialkow, MD, MPH, is Director of the Resident Surgical Skills Curriculum.

Training Assessment Sites

The SERP Program is run in three environments:

1) Self-directed learning occurs wherever and whenever the resident has time to practice. ISIS lab is accessible by the residents 24 hours/7 days per week to allow for independent practice at the convenience of the resident.
2) Directed 2-hour dry labs are scheduled in the ISIS Center and use models, simulators, skills drills, etc. for training and evaluation. ISIS labs are held several times per year. Additional curricula are undergoing development with ISIS faculty experts.
3) The 3-hour porcine model lab allows training and evaluation of several Ob/Gyn procedures and is held once a year.

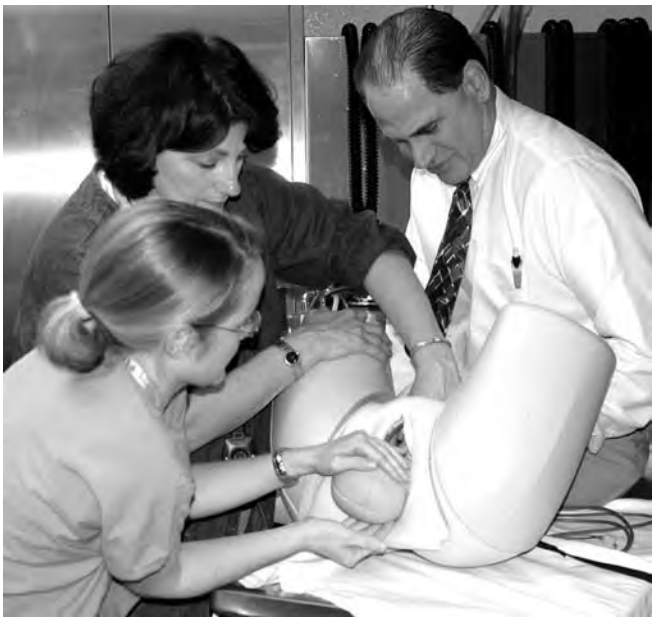
Education and Training

RESIDENCY PROGRAM

Center for Videoendoscopic Porcine Surgery Training Lab

Our Ob/Gyn training program has a nationally recognized surgical skills curriculum and simulation lab, providing an alternative to training on patients. This comprehensive surgical skills curriculum uses a combination of two-on-one surgical training in the University of Washington's ISIS ("Dry Lab") with practice and testing on anesthetized pigs (Videoendoscopic Porcine Surgery Training Lab). As a national model for best practices, it is dedicated to providing a highly collaborative education and training environment in the area of minimally invasive surgery, as well as training residents, fellows, and practicing surgeons from around the world.

Institute for Simulation and Interprofessional Studies (ISIS)



The primary goal of the University of Washington's Institute for Simulation and Interprofessional Studies is to provide leadership in the use of simulation technologies to improve the quality of health care education, patient safety and outcomes. Our nationally recognized ISIS Center has placed UWMC at the "virtual" cutting edge in surgical skills and simulation. It is conveniently located on the first floor of the University of Washington Medical Center's Surgery Pavilion.

This curriculum has moved into the next phase of development to provide training on the management of OB hemorrhage scenarios such as postpartum hemorrhage, shoulder dystocia, and eclamptic seizure, as well as training on disclosing adverse medical events. The curriculum includes both training and assessment of com-petency in all areas.

This center received accreditation as a Level 1 Comprehensive Education Institute of the American College of Surgeons in 2006.
Refer to our ISIS website for more details: http://www.isis.washington.edu/

Education and Training

2010–2011 GRAND ROUNDS—First Half

September 15: **Magnesium for Neuroprotection of the Preterm Infant**
Shani S Delaney, MD, F2 Maternal-Fetal Medicine Fellow, Department of Obstetrics and Gynecology, University of Washington

September 22: **The Progestin-Containing Intrauterine Device: More Than Just a Contraceptive**
Laura Cieslik, MD, R4 Resident Physician, Department of Obstetrics and Gynecology, University of Washington

September 29: **Obstetrical Malpractice**
Joel Cunningham, JD, Partner; Luvera, Barnett, Brindley, Beringer & Cunningham; Seattle, WA

October 6: No Grand Rounds

October 13: **The Ethical Dilemma: Personal Choices in Infertility Treatments**
Paul W Zarutskie, MD, Acting Associate Professor, Division of Reproductive Endocrinology & Infertility, Department of Obstetrics and Gynecology, University of Washington

October 20: **One Year Continuation & Unintended Pregnancy in Adolescents & Young Women**
Tina Raine-Bennett, MD, MPH. Professor; Obstetrics, Gynecology & Reproductive Sciences; University of California, San Francisco

October 27: **PRONTO: Innovation in Emergency Obstetric Training for Resource Limited Settings**
Dilys M Walker, MD, Associate Professor, Women's Health—Harborview Medical Center, Department of Obstetrics and Gynecology, University of Washington

November 3: **Assisted Reproductive Technology: Past, Present and Our Future**
Jacob F Mayer, Jr, PhD, Professor, Jones Institute for Reproductive Medicine, Department of Obstetrics and Gynecology, East Virginia Medical School, Norfolk, VA

November 10: **Career, Family and Life: Exploring Rural Medicine**
Shawni L Coll, DO, Volunteer Clinical Faculty, Ob/Gyn Clerkship Director, Chair of Ob/Peds Department, UC Davis School of Medicine, Tahoe Forest Hospital

November 17: **Uterine Artery Interventions**
Siddarth A Padia, MD, Assistant Professor, Vascular and Interventional Radiology, University of Washington

November 24: No Grand Rounds

December 7: **Vaginal Birth After Cesarean—National and Local Insights**
Anna R Shope, MD, R4 Resident Physician, Department of Obstetrics and Gynecology, University of Washington

December 8: **From PubMed to the Public: Where Do Epidurals Get Lost in Translation?**
Ruth Landau, MD, Professor, Department of Anesthesiology & Pain Medicine, University of Washington

December 15: **Improving US Health Care Delivery**
Hugh M Foy, MD , Professor, Department of Surgery; HMC Trauma and Critical Care Division; Director, Surgical Specialties Clinic, Harborview Medical Center; University of Washington

Education and Training

RESIDENT & FELLOW RESEARCH DAY

2010 Senior Resident Research Presentations

Leslie Carranza, MD:	Training of Ob/Gyn Residents in the Disclosure of Adverse Events and Medical Errors: A Randomized Study of Traditional Didactic Teaching vs. Training with Standardized Patients
Merry (Ali) Lewis, MD:	Postpartum IUD Use: Factors Associated with Not Receiving a Planned Postpartum IUD
Katherine A McLean, MD:	Ovarian Cancer in the Elderly: Outcomes with Neoadjuvant Chemotherapy or Primary Cytoreduction
Leslie C McLemore, MD:	Long-Term Effect of Depomedroxyprogesterone on Vaginal Flora, Epithelium and Immune Cells
Elizabeth E Tenpenny, MD:	Fetal Lung Maturity Testing: Predictor of Overall Neonatal Outcomes?
Chad B Thomas, MD, PhD:	Pregnancy Rates from Lead Follicles

2010 Fellow Research Presentations

Suzanne E Peterson, MD:	Prospective Assessment of Feto-Maternal Cell Trafficking in Abortion
Kerry M McMahon, MD:	Abnormal Placentation and the Role of Soluble fms-Like Tyrosine Kinase 1 (sFlt-1)
Chirag A Shah, MD, MPH:	Results of a Prospective Screening Trial in Women at Increased Risk of Ovarian Cancer Utilizing the Parametric Empiric Bayes (PEB) Algorithm

2009 Senior Resident Research Presentations

Justine C Chang, MD:	LPS Variants Differentially Stimulate Inflammatory Responses in Macaque Fetal Membranes
Katherine E Debiec, MD:	Inadequate Prenatal Care and Risk of Preterm Delivery Among Adolescents: A Retrospective Study Over 10 Years
Alison (Ali) G DeSano, MD:	Success of Letrozole Treatment after Clomiphene Failure
Sue J Lee, MD:	Loop Electrosurgical Excisional Procedure (LEEP) Done for Discrepancy: Does the Time from HGSIL Affect Pathologic Grade of CIN in LEEP Specimen?
Wendy J Lorentz, MD:	Maternal and Fetal Outcomes with Progesterone Use for the Prevention of Preterm Labor
Olivia M Sementi, MD:	The Mirena IUD: Prescribing Practices and Beliefs Among Seattle Family Physicians and Obstetrician/Gynecologists

2009 Fellow Research Presentations

Ruchi Garg, MD:	Human Papillomavirus Serology in Anal Cancer
Drew Robilio, MD:	Diagnosis of Early-Onset Neonatal Sepsis in Premature Neonates from Proteomic Analysis of Umbilical Cord Blood

Education and Training

RESIDENCY PROGRAM

What Our Graduates Are Doing

2010 Graduates	***Medical School***	***Career After Residency***
Carranza, Leslie	Minnesota	Academic medicine (UW)
Lewis, Merry (Ali)	UW	Academic medicine (UW)
McLean, Kate	Chicago /Pritzker	Gyn Onc fellowship, UW
McLemore, Leslie	St. Louis	Private practice (Yakima, WA)
Tenpenny, Elizabeth	UW	Private practice (Seattle, WA)
Thomas, Chad	Illinois Urbana/Cham	Private practice (Bellingham, WA)
2009 Graduates		
Chang, Justine	Brown	Maternal-Fetal Medicine fellowship, Magee-Womens Hospital
Debiec, Katherine	UW	Academic medicine, UW
DeSano, Ali	UW	Private practice (Salt Lake City, Utah)
Lee, Sue	Columbia	Academic medicine, UW
Lorentz, Wendy	UW	Academic medicine, UW
Sementi, Olivia	UW	Private practice (Spokane, WA)
2008 Graduates		
Marrs, Jessie	UW	Private practice (Seattle, WA)
Nathan, Joshua	George Washington Univ	Private practice (Everett, WA)
Norland, Emily	Iowa	Private practice (Seattle, WA)
Norquist, Barbara	UW	Gyn Onc fellowship, UW
Simmons, LaVone	Vermont	Academic medicine, UW
Stephenson-Famy, Alyssa	UW	Maternal-Fetal Medicine fellowship, Magee-Womens Hospital
2007 Graduates		
Aryal, Prashanti	Illinois	Private practice (Seattle, WA)
Walker, Kym	Rochester	Private practice (Olympia, WA)
Piggott, Dionne	North Carolina	Private practice (North Carolina)
Fox, Katrina	VA Commonwealth	UW academic faculty, then private practice (NC)
Unger, Jennifer	Connecticut	UW academic faculty/WRHR Scholar
Kurachi, Akiko	Michigan	Private practice (Seattle, WA)
2006 Graduates		
Ackerman, Diana	UC Irvine	Private practice (Bend, OR)
Fowler, Julia	Tulane	Private practice (Portland, OR)
Lamb, Julie	Northwestern	REI fellowship, UCSF
Memmel, Lisa	Wisconsin	Family Planning fellowship, Chicago
Mitchell, Caroline	Harvard	UW academic faculty/WRHR Scholar
Shah, Chirag	Indiana	Gyn Onc fellowship, UW

Education and Training

FELLOWSHIP PROGRAM

Gynecologic Oncology *(4 years)*

Barbara A Goff, MD, Director, Gynecologic Oncology Fellowships

Training fellows in the comprehensive management of gynecologic malignancies and research through clinical and research mentors. Based primarily at UWMC and Seattle Cancer Care Alliance, including rotations at Swedish Hospital Medical Center.

F4	Joshua Z Press, MD, MSc	University of British Columbia *(Residency)* University of British Columbia *(MSc)* University of Alberta *(MD)*
F3	Barbara M Norquist, MD	University of Washington *(Residency)* University of Washington *(MD)*
F2	Melissa M Thrall, MD	University Health Center of Pittsburgh/ Magee-Womens Hospital *(Residency)* Albany Medical College *(MD)*
F1	Katherine A McLean, MD	University of Washington *(Residency)* University of Chicago/Pritzker *(MD)*

Website: http://www.depts.washington.edu/obgyn/EducationFiles/Education.html

Maternal-Fetal Medicine *(3 years)*

Jane E Hitti, MD, MPH, Director, Maternal-Fetal Medicine Fellowships

Designed to give fellows a well-rounded experience in Maternal-Fetal Medicine, with time equally divided between clinical experience and research in preparation for a productive career in either academic medicine or private perinatal practice.

F3	Sophia M Rothberger, MD, MPH	Oregon Health & Science University *(Residency)* University of North Carolina *(MPH, Epi)* University of North Carolina *(MD)*
F3	Sarah A Waller, MD	Stanford University *(Residency)* Tulane University SOM *(MD)*
F2	Shani S Delaney, MD	University of California, San Francisco *(Residency)* University of California, San Francisco *(MD)*
F1	Eve M Bernstein, MD	Yale New Haven *(Residency)* University of Alabama *(MD)*
F1	Jeroen P Vanderhoeven, MD	Oregon Health & Science University *(Residency)* Drexel University *(MD)*

Website: http://www.depts.washington.edu/obgyn/EducationFiles/Education.html

Education and Training

MEDICAL STUDENTS

Overview

A core mission of the University of Washington School of Medicine is to educate students who will likely provide medical care for five of the states within District VIII: Washington, Wyoming, Alaska, Montana, and Idaho (WWAMI). UW's philosophy is to focus on decentralizing medical education within the WWAMI region, and to involve District VIII Fellows in the teaching process. Approximately 60% of students will complete their clerkship at sites distant from the Seattle area.

Through the cooperative work of the UW Department of Ob/Gyn faculty in Seattle and community faculty composed of ACOG Fellows and Junior Fellows, the program has become a nationally recognized educational model. with 60% of UW students eventually practicing within the five-state WWAMI region.

- **Required 3rd-Year Ob/Gyn Clerkship**

  During this 6-week required core clerkship, students will have the opportunity to interact with women in all stages of life, experience a variety of obstetrical and gynecologic conditions in both outpatient and inpatient settings, participate in the care of laboring patients, attend deliveries and gynecologic surgeries, and gain an understanding of the primary care mission within our specialty. As in all core clerkships, students will learn many valuable skills during this rotation to help them develop into self-directed, life-long learners.
  Website: http://www.obgyn.uwmedicine.org/clerkship

- **4th-Year Electives** *(4 weeks each)*

  681P: Gynecologic Oncology
  Students will acquire basic surgical skills and be exposed to evaluation, counseling, adjuvant therapies, and complex surgical procedures, care for multiple medically complicated patients simultaneously, and work with multidisciplinary teams in the care of gynecologic oncology patients.

  682P: Antenatal High-Risk Obstetrics
  Students will learn to evaluate and manage medically complicated patients and common pregnancy complications, learn the effect of common medical diseases on the course of pregnancy and the effect of pregnancy on the course of these diseases.

  685: Subspecialty Gynecology
  Students are exposed to the breadth and depth of specialty areas of gynecology, including urogynecology, family planning, adolescent gynecology, and reproductive endocrinology and infertility.

  Obstetrics and Gynecology Special Electives
  By special arrangement and permission, special clerkship, externship, or preceptorship opportunities can at times be made available at other institutions or private offices (Course 697P) or sites within the WWAMI region (Course 699P)

Education and Training

CAREER DEVELOPMENT AWARDS

Women's Reproductive Health Research (WRHR) Career Development Program
David A Eschenbach, MD, Principal Investigator
Susan M Reed, MD, MPH, Research Program Director
Elizabeth M Swisher, MD, Scientific Advisor

Since 1999, the UW's Department of Obstetrics and Gynecology has been funded by the National Institutes of Health as a Women's Reproductive Health Research Career Development Training Center. The long-term goal is to recruit and facilitate the career development of obstetrician gynecologists who have demonstrated research potential and are committed to a career in academic medicine.

The principle training format is a mentored experience with a successful investigator *(clinical or basic research)* for a minimum of two, but up to five, years. During this period, the scholar devotes 75–80% of their time to research. The research scope is open for the scholar and mentor to direct, and encompasses all areas of obstetrics and gynecology and its subspecialties. The UW Ob/Gyn Department can support a maximum of four scholars at any given time.

- ***Currently Funded Scholars***

  Hilary S Gammill, MD, Maternal-Fetal Medicine *(January 2007–December 2011)*
  — Immunologic Maladaptation and Microchimerism in Preeclampsia

- ***Scholars Who Have Already Completed WRHR Training***

  Caroline M Mitchell, MD, MPH, Women's Health *(August 2006–April 2010)*
  — HIV-1 in the Female Genital Tract

  Jennifer A Unger, MD, MPH, Women's Health *(August 2007–April 2009)*
  — The Immunologic Factors Involved in Adverse Pregnancy Outcomes Related to Malarial Infection

  Michael F Fialkow, MD, MPH, Female Pelvic Medicine and Reconstructive Pelvic Surgery *(July 2004–July 2007)*
  — Epidemiology of Recurrent Pelvic Organ Prolapse

  Kristina M Adams Waldorf, MD, Women's Health *(July 2002–December 2006)*
  — The Maternal-Fetal Immune Response to Preterm Labor

  Jennifer L Melville, MD, MPH, Women's Health *(July 1999–March 2004)*
  — Depression and Obstetric-Gynecologic Disorders

  Elizabeth M Swisher, MD, Gynecologic Oncology *(July 1999–September 2002)*
  — Molecular Markers in Ovarian Cancer

  Susan D Reed, MD, MPH, Women's Health *(July 1999–July 2001)*
  — Steroid Hormones and Uterine Neoplasms

  S Samuel Kim, MD, Reproductive Endocrinology and Infertility *(July 1999–July 2001)*
  — Ovarian Cryopreservation and Transplantation

Website: http://www.depts.washington.edu/obgyn/EducationFiles/Education.html

PATIENT CARE

Division of GYNECOLOGIC ONCOLOGY

The Gyn Onc Division strives to provide the best comprehensive gynecologic oncology care available to patients with gynecologic cancers. The six gynecologic oncologists in this division, all of whom are sub-specialty certified, constitute the largest single group of gynecologic oncologists in the Pacific Northwest. Dr. Hipps joined the division in 2008 to provide gynecologic support for cancer patients at the SCCA. In addition, four Gyn Onc Fellows are in training.

In 2008, over 850 new reproductive tract cancer patients were seen in the Gynecologic Oncology Clinic at the Seattle Cancer Care Alliance (SCCA) Southeast Lake Union facility, an alliance of UWMC, Children's Hospital & Regional Medical Center, and the Fred Hutchinson Cancer Research Center. Over 460 major surgical cases and 175 minor surgeries were performed, plus ~750 cycles of chemotherapy administered. The service continues to grow.

Barbara A Goff, MD
Professor & Director, Gyn Onc
Univ of Pennsylvania (MD)
Brigham & Wmn's Hosp (Res)
Mass General Hosp (Gyn Onc)

Heidi J Gray, MD
Asst Prof, Gynecologic Oncology
Univ of California LA (MD)
University of Washington (Res)
Univ of Pennsylvania (Gyn Onc)

Benjamin E Greer, MD
Prof, Gynecologic Oncology
Univ of Pennsylvania (MD)
University of Colorado (Res)

Linda Joy Hipps, MD
Clin Assoc Prof, Gyn Onc
Catholic Univ Louvain (MD)
Winthrop Univ Hosp (Res)

Ron E Swensen, MD
Assoc Prof, Gyn Onc & Education
Loma Linda University (MD)
Stanford University (Res)
Hershey Med Ctr (Gyn Onc)

Elizabeth M Swisher, MD
Assoc Prof, Gynecologic Oncology
Univ of Calif, San Diego (MD)
University of Washington (Res)
Washington University (Gyn Onc)

Hisham K Tamimi, MD
Prof, Gynecologic Oncology
Cairo University (MD)
Northwestern University (Res)
Memorial Sloan-Kettering (Gyn Onc)

Barbara J Silko, PhD, ARNP
Teaching Associate
Univ Wisconsin, Madison (BSN)
Univ Wisconsin, Eau Claire (MSN)
Univ of Washington (PhD)
Univ of Washington (ARNP)

Photo Unavailable

Elizabeth Anderson, ARNP, MSN
Teaching Associate
Seattle University (BSN)
xxxxx (MSN)
xxxxx (ARNP)

Joshua Z Press, MD, MSc
Fourth Year Fellow (Gyn Onc)
Univ of Alberta, Canada (MD)
Univ of British Columbia (Res)

Barbara M Norquist, MD
Third Year Fellow (Gyn Onc)
University of Washington (MD)
University of Washington (Res)

Melissa M Thrall, MD
Second Year Fellow (Gyn Onc)
Albany Medical College (MD)
Magee-Women's Hosp (Res)

Katherine A McLean, MD
First Year Fellow (Gyn Onc)
Univ of Chicago/Pritzker (MD)
University of Washington (Res)

Division of GYNECOLOGIC ONCOLOGY

Seattle Cancer Care Alliance (SCCA)

The Seattle Cancer Care Alliance is a collaboration between
— Fred Hutchinson Cancer Research Center
— University of Washington
— Seattle Children's Hospital
Its purpose is to facilitate the flow of scientific information between researchers, clinicians and patients in hopes of accelerating the research process and, ultimately, the development of more effective cancer treatments.

Appointments: (206) 288-6200
FAX: (206) 288-6268

Hours: Monday–Thursday, 9:00–4:00
Friday, 10:00–3:00

Location: 825 Eastlake Avenue East
Seattle, WA 98109

Website: http://www.seattlecca.org

Services: Multidisciplinary clinic for all gynecologic cancers
- Cervical
- Choriocarcinoma
- Endometrial
- Fallopian tube
- Gestational trophoblastic disease
- Ovarian
- Paget's disease
- Uterine
- Vaginal
- Vulvar

Facilities: In addition to our comprehensive outpatient clinical facilites at the Seattle Cancer Care Alliance site, the UW Medical Center has three adult hematology/oncology units totaling 86 beds, and newly constructed, state-of-the-art outpatient clnic space for hematology/oncology patients.

Division of MATERNAL-FETAL MEDICINE

The Division of Maternal-Fetal Medicine provides quality patient care, conducts extensive medical education, and performs clinical and basic research. It is composed of eleven faculty, including seven subspecialty certified in maternal-fetal medicine out of eight who are eligible and one who is an active candidate for subspecialty certification; five maternal-fetal medicine fellows; five certified nurse midwives; a PhD diabetes clinical nurse specialist; and two perinatal clinical nurse specialists. We specialize in high-risk obstetrics, including hypertension in pregnancy, diabetes in pregnancy, multiples, prematurity prevention, and prenatal diagnosis and fetal therapy.

Maternal-fetal medicine services are also offered at Providence Everett Medical Center, Yakima Valley Memorial Hospital, Columbia Health Center, and the Prenatal Diagnosis and Treatment Program at Seattle Children's Hospital.

Michael G Gravett, MD
Professor and Director,
Maternal-Fetal Medicine
Univ of California, LA (MD)
University of Washington (Res)
University of Washington (MFM)

Donald AG Barford, MD
Clinical Prof, Mat-Fet Med
University of London (MD)
Univ of Natal, South Africa (Res)
Case Western Reserve (MFM)

Thomas J Benedetti, MD, MHA
Prof, Maternal-Fetal Medicine
Director, Division of Education
University of Washington (MD)
Univ of Southern California (Res)
Univ of Southern California (MFM)

Zane A Brown, MD
Prof, Maternal-Fetal Medicine
Assoc Residency Prgrm Director
Temple University (MD)
University of Utah (Res)
University of Utah (MFM)

Edith Y Cheng, MD, MS
Prof, Maternal-Fetal Medicine
Assoc Div Dir, Clin Operations
University of Washington (MD)
University of Washington (Res)
UW (MFM & Med Genetics)

Thomas R Easterling, MD
Prof, Maternal-Fetal Medicine
Univ of North Carolina (MD)
Oregon Hlth & Science Univ (Res)
University of Washington (MFM)

Hilary S Gammill, MD
Asst Prof, Mat-Fet Medicine
University of Washington (MD)
Univ of Pittsburgh (Res)
Univ of Pittsburgh (MFM)

Jane E Hitti, MD, MPH
Prof, Maternal-Fetal Medicine
University of Vermont (MD)
Med Ctr Hosp of Vermont (Res)
Univ Wash (MFM/Infect Disease)

Emily V Holing, PhD, ARNP
Teaching Associate
University of Washington (BS)
University of Washington (MA)
University of Washington (PhD)

Kathleen Kenny, ARNP, CNM, MA, *Teaching Assoc*
University of Vermont (BSN)
New York Univ (MA Midwif)

Kathy O'Connell, MN, RN
Clinical Instructor
Perinatal Clinical Nurse Specialist
Univ of California, LA (MN)
State Univ of NY College (BSN)

Patient Care & Clinical Services

Division of MATERNAL-FETAL MEDICINE

Sophia M Rothberger, MD, MPH
Acting Instructor, Mat-Fet Med
Third Year Fellow (MFM)
Univ of North Carolina (MPH)
Univ of North Carolina (MD)
Oregon Hlth & Science Univ (Res)

Sarah A Waller, MD
Acting Instructor, Mat-Fet Med
Third Year Fellow (MFM)
Tulane University (MD)
Stanford University (Res)

Shani S Delaney, MD
Acting Instructor, Mat-Fet Med
Second Year Fellow (MFM)
Univ Calif, San Francisco (MD)
Univ Calif, San Francisco (Res)

Eve M Bernstein, MD
Acting Instructor, Mat-Fet Med
First Year Fellow (MFM)
University of Alabama (MD)
Yale New Haven Hosp (Res)

Jeroen P Vanderhoeven, MD
Acting Instructor, Mat-Fet Med
First Year Fellow (MFM)
Drexel University (MD)
Oregon Hlth & Science Univ (Res)

Bonnie L Bernstein,
CNM, MSN, ARNP
Teaching Assoc/Certified Nurse
Midwife, Maternal-Fetal Med
California State University (BS)
Columbia University (MS)

Mary T Bolles,
CNM, MSN, ARNP
Teaching Assoc/Certified Nurse
Midwife, Maternal-Fetal Med
University of Washington (BS)
University of Washington (MN)

Michelle M Grandy,
CNM, MSN, ARNP
Teaching Assoc/Certified Nurse
Midwife, Maternal-Fetal Med
Seattle Pacific University (BS)
University of Washington (MS)

Robyn L Holloman,
CNM, ARNP
Teaching Assoc/Certified Nurse
Midwife, Maternal-Fetal Med
University of Washington (BS)
University of Washington (MN)

Cynthia R Rogers,
CNM, MSN
Teaching Assoc/Certified Nurse
Midwife, Maternal-Fetal Med
Eastern Washington Univ (BS)
Case Western Reserve Univ (MS)

Division of MATERNAL-FETAL MEDICINE

Maternal and Infant Care Clinic (MICC)

In September 2009, the University of Washington Medical Center was designated as a "Baby Friendly Hospital", a WHO/UNICEF designation for hospitals that meet a specified 10 Steps to Baby Friendly. The 10 steps are all actions that promote maternal newborn interaction in general and breastfeeding specifically. UWMC is the only Seattle area hospital to be awarded this designation, the 5th hospital in the State of Washington, and one of the few academic medical centers nationally to achieve Baby Friendly status.

The MICC provides a complete range of services for pregnant women and their developing babies.

Appointments: (206) 598-4070
FAX: (206) 598-4694

Hours: Monday–Friday, 8:00 am–5:00 pm

Location: University of Washington Medical Center *(3rd floor)*
1959 NE Pacific Street (Box 356159)
Seattle, WA 98195

Website: http://www.uwbaby.org

Services: Specialty clinics and programs:
- Breastfeeding support
- Diabetes in Pregnancy Clinic
- Fetal Medicine/Ultrasound
- Midwifery
- Obstetrical Hypertension Consult Clinic
- Obstetrics—high-risk and routine
- Prematurity Prevention Program and Multiple Gestation Clinic
- Prenatal Genetics and Fetal Therapy Service
- Perinatal Education classes

Facilities: The MICC has 16 exam rooms, 2 NST beds, Ultracom services and 2 ultrasound rooms for patient convenience. They recently upgraded their fetal monitoring capacity to be able to monitor triplets and up to 5 patients at a time.

A major remodel combining antepartum facilities and Labor & Delivery into one unit on the sixth floor was completed in 2002. Each antepartum room has a TV, VCR, CD player, refrigerator, rocking chair, private bathroom and daybed. There are nine labor/delivery/recovery (LDR) rooms, each with the above amenities, including whirlpool tub in the private bathrooms. All antepartum and LDR beds are connected to central monitoring.

The Postpartum unit on the fifth floor has a five-bed newborn nursery and 18 private rooms, all with the same amenities as Antepartum and Labor & Delivery.

UWMC has broken ground on a new building opening in 2012 which will incorporate a new 50-bed NICU, accessible from the main hospital via a sky bridge.

Division of REPRODUCTIVE ENDOCRINOLOGY AND INFERTILITY

The Division of Reproductive Endocrinology and Infertility (REI) is composed of three physicians and three basic scientists with NIH grants. The Department of Obstetrics and Gynecology is in the process of recruiting a division director and additional clinical faculty.

Brenda S Houmard, MD, PhD
Clin Asst Prof, Repro Endo & Infer
Ohio State University (PhD)
Ohio State University (MD)
Ohio State University (Res)
University of Washington (REI)

Kathleen Lin, MD
Asst Prof, Repro Endo & Infer
Albert Einstein College (MD)
NY Pres Hosp/Cornell Med Ctr (Res)
Univ of Pennsylvania (REI)
Cornell Med Ctr (Male Infertility)

Paul W Zarutskie, MD
Act Assoc Prof, Repro Endo & Infer
Hahnemann Med Coll (MD)
Duke University (Res)
Brigham & Wmn's, Harvard (REI)

University Reproductive Care *(at Women's Health Care Center, Roosevelt)*

4245 Roosevelt Way NE, 3rd floor

Website: http://www.obgyn.uwmedicine.org/URC

Services:

- **Reproductive Endocrine Care**
  - — Recurrent pregnancy loss
  - — Polycystic ovarian disease
  - — Endometriosis
  - — Endocrinopathies
  - — Androgen excess syndromes
  - — Menstrual disorders
  - — Metabolic disorders
- **Comprehensive Fertility Program**
  - — Ovulation induction
  - — Intrauterine inseminations
  - — Assisted Reproductive Technologies (ART)
- **Techniques/Procedures**
  - — Advanced laparoscopy/hysteroscopy
  - — Correction of Müllerian anomalies
  - — Fertility preservation surgical training
  - — Reproductive imaging training (ultrasound/radiologic)
  - — Microsurgical sperm retrieval
  - — Microsurgical tubal anastomosis
- **Fertility Preservation**
  - — Pediatric/adolescent/adult care
  - — Gamete/embryo/tissue cryopreservation for oncology/chronic disease states

Patient Care & Clinical Services

Division of WOMEN'S HEALTH CARE

The University of Washington Medical Center (UWMC) **Women's Health Care** faculty members provide preventive, obstetric and gynecologic care for women, including routine and high-risk obstetrics, family planning services, minimally invasive surgery, and specialized gynecologic care. They are also responsible for supervising and teaching in the residents' gynecology clinics (PGY1 and PGY4) and resident continuity clinics at Roosevelt Women's Health Care Clinic. They provide specialty care for a wide range of conditions that affect women, such as abnormal uterine bleeding, endometriosis, premalignant disease of the lower genital tract, benign gynecologic tumors, pelvic pain, and menopausal issues.

David A Eschenbach, MD
Chair, Department of Ob/Gyn
Professor, Women's Health
University of Washington (MD)
University of Washington (Res)
Univ of Wash (Infectious Disease)

Seine Chiang, MD
Associate Professor
Div Director, UWMC Wmn's Hlth
Residency Program Director
Oregon Hlth & Science Univ (MD)
University of Texas (Res)

Kristina Adams Waldorf, MD
Asst Professor, Women's Health
Mayo Medical School (MD)
University of Washington (Res)

Katherine E Debiec, MD
Acting Instructor, Wmn's Hlth
University of Washington (MD)
University of Washington (Res)

Rebecca Dunsmoor-Su, MD, MSCE
Asst Professor, Women's Health
Univ of Pennsylvania (MD)
Univ of Pennsylvania (MSCE)
Univ of Pennsylvania (Res)

Carolyn Gardella, MD, MPH
Assoc Professor, Women's Hlth
Gyn Chief, VA Puget Sound
State University of NY (MD)
University of Washington (Res)
Univ of Washington (MPH, Epi)

Merry (Ali) Lewis, MD
Clin Asst Prof, Wmn's Hlth
University of Washington (MD)
University of Washington (Res)

Wendy J Lorentz, MD
Clinical Instructor, Wmn's Hlth
University of Washington (MD)
University of Washington (Res)

Vicki Mendiratta, MD
Assoc Professor, Women's Hlth
Ob/Gyn Clerkship Director
Ohio State University (MD)
Ohio State University (Res)

Sue Lee Moreni, MD
Acting Asst Prof, Wmn's Hlth
Columbia University (MD)
University of Washington (Res)

Anne-Marie Amies Oelschlager, MD
Asst Professor, Women's Health
Vanderbilt University (MD)
University of Washington (Res)

Sarah W Prager, MD, MAS
Asst Prof, Women's Health
University of Texas (MD)
University of Vermont (Res)
Univ of Calif, SF (Fam Plan)

LaVone E Simmons, MD
Clin Instructor, Wmn's Hlth
University of Vermont (MD)
University of Washington (Res)

Patient Care & Clinical Services

WOMEN'S HEALTH CARE Practice Sites

Appointments

• **Women's Health Care Clinic, Roosevelt** (206) 598-5500
4245 Roosevelt Way NE, 3rd floor
Seattle, WA 98105

— Ob and Gyn practice *(Drs. Dunsmoor-Su, Lorentz, Mendiratta, Moreni, Simmons)*
— Gyn-only practice *(Drs. Chiang, Adams-Waldorf, Eschenbach, Oelschlager)*
— Vulvovaginitis Clinic *(Dr. Eschenbach)*
— Dysplasia Clinic *(Dr. Chiang)*
— Women's Options Center *(Dr. Prager)*

http://www.uwmedicine.org/PatientCare/MedicalSpecialties/PrimaryCare/UWMedicalCenter/WHCC/

• **Maternal and Infant Care Clinic (MICC) Teen OB Clinic** *(Dr. Debiec)* (206) 598-4070
University of Washington Medical Center (3rd floor)
1959 NE Pacific Street
Seattle, WA 98195

http://www.uwbaby.org

• **OB Teaching Laborists** *(Drs. Dunsmoor-Su, Lewis, Mendiratta)* (206) 598-4616

• **Seattle Children's Hospital**
Pediatric and Adolescent Gynecology Clinic *(Drs. Debiec, Oelschlager)* (206) 987-2028
4800 Sand Point Way NE
Seattle, WA 98105

http://www.seattlechildrens.org/clinics-programs/adolescent-gynecology/your-care-team/

• **UWPN Shoreline Clinic** *(Drs. Lorentz, Simmons)* (206) 542-5656
1355 North 205th Street
Shoreline, WA 98133

http://uwmedicine.washington.edu/Facilities/NeighborhoodClinics/Clinics/Shoreline/

• **VA Women's Health Care Centers**
— **Puget Sound** *(Dr. Gardella)* (206) 768-5314
1660 South Columbian Way
Seattle, WA 98108-1532
— **American Lake** *(Drs. Moreni, Shy)* (253) 589-4045
9600 Veteran's Drive
Tacoma, WA 98493

http://www1.va.gov/pugetsound/page.dfm?pg=242

Patient Care & Clinical Services

Division of WOMEN'S HEALTH CARE

Harborview Women's Clinic offers a wide range of obstetric, gynecologic and primary care services, with active inpatient and outpatient gynecologic surgical services. Harborview is the site of the Northwest regional trauma and burn centers, the Center for Sexual Assault and Traumatic Stress, and is also the county hospital for King County, serving all women, regardless of socioeconomic status or ethnicity.

Susan D Reed, MD, MPH
Professor, Women's Health
Div Director, HMC Wmn's Hlth
Stanford University (MD)
Univ of California, SF (Res)
Univ of Washington (MPH, Epi)

Leslie Carranza, MD
Acting Asst Prof, Wmn's Hlth
University of Minnesota (MD)
University of Washington (Res)

Linda O Eckert, MD
Assoc Prof, Women's Health
Gyn Director, Harborview
Sexual Assault Center
Univ of Calif, San Diego (MD)
University of Texas (Res)
Univ of Washington (Infect Dis)

Constance Mao, MD
Asst Prof, Women's Health
Dir, HMC Wmn's Colposcopy Clinic
Univ of Southern Calif, LA (MD)
University of Washington (Res)

Jennie Mao, MD
Acting Asst Prof, Wmn's Hlth
University of Michigan (MD)
Univ of New Mexico (Res)

Caroline Mitchell, MD, MPH
Asst Prof, Women's Health
Harvard Medical School (MD)
University of Washington (Res)
Univ of Wash (MPH, Epi)

Kirkwood K Shy, MD, MPH
Professor, Women's Health
Wayne State University (MD)
University of Washington (Res)
Univ of Wash (MPH, Hlth Srvcs)

Dilys M Walker, MD
Assoc Prof, Women's Hlth
Univ of Calif, San Diego (MD)
University of Pennsylvania (Res)
Buffet Fam Foundation (Fam Plan)

Patient Care & Clinical Services

Division of WOMEN'S HEALTH CARE

Harborview Women's Clinic

Appointments: (206) 731-3367
FAX: (206) 731-2873

Hours: Monday, Wednesday, Thursday, Friday, 8:00 am–5:00 pm
Tuesday, 8:00 am–6:00 pm

Location: Harborview Medical Center *(ground floor, west clinic)*
325 Ninth Avenue
Box 359854
Seattle, WA 98104-2499

Website: http://www.uwmedicine.org/PatientCare/MedicalSpecialties/PrimaryCare/Harborview/Women/

Services: Clinics:
- Dysplasia
- General Gynecology
  - — Abnormal bleeding
  - — Fibroids
  - — Endometriosis
  - — Ovarian cysts
  - — Sexually transmitted diseases (STDs)
  - — Pelvic relaxation
- General Obstetrics
  - — Family planning and birth control options
- Refugee and Immigrant
  - — Post-traumatic stress
  - — Genital circumcision

Patient Care & Clinical Services

Division of UROGYNECOLOGY

Gretchen M Lentz, MD
Professor and Director, Urogynecology
University of Washington (MD)
University of Washington (Res)
St George's Hosp, London (Urogyn)

Michael F Fialkow, MD, MPH
Asst Prof, Urogynecology, Educ Dir, Resident Surg Skills Curriculum
University of Washington (MD)
University of Washington (Res)
University of Washington (Urogyn)
Univ of Washington (MPH, Epi)

Urogynecology Clinic, UWMC Surgery Pavilion
Physicians at the University of Washington and throughout the Pacific Northwest refer patients to the two urogynecologists in this division for the diagnosis and treatment of complicated uterovaginal prolapse, pelvic relaxation, urinary and fecal incontinence, and fistulas. Our two urogynecologists also work closely with the Female Pelvic Medicine and Reconstructive Surgery (FEPMARS) group, which includes one urologist and a nurse practitioner specializing in female urology. The entire group evaluates >500 new patients, and performs 200 urodynamic studies and 300 surgeries per year.

Appointments: (206) 598-5960
FAX: (206) 598-6986

Hours: Monday 8:00–5:00
Wednesday 1:00–5:00
Thursday 9:00–5:00
Friday 8:00–5:00

Location: University of Washington Medical Center *(1st floor)*
1959 NE Pacific Street
Box 356158
Seattle, WA 98195

The Surgery Pavilion is located at the east end of University of Washington Medical Center, connected to the main building by a glass footbridge. The Urology Clinic is on the first floor, to the left and through the glass doors as you come down the stairs or get off the elevator.

Website: http://www.uwmedicine.org/Facilities/UWMedicalCenter/Overview/SurgeryPavilion/

Services:
- Pelvic organ prolapse
- Pelvic floor reconstructive surgery for prolapse
- Urinary incontinence
- Fecal incontinence
- Fistulas
- Robotic surgery

RESEARCH

Research

CAREER DEVELOPMENT

Research Training Centers for Physicians in Women's Health (K12)

David A Eschenbach, MD, Principal Investigator

WRHR at UW, a medical residency in Ob/Gyn, is an intense four-year clinical experience, sometimes followed by a three-year, subspecialty fellowship. Physicians who complete a residency and/or fellowship are usually superb clinicians, but generally are not well prepared to meet the research requirements. This proposal describes a plan for a continuation of a successful Research Career Development Center in women's health for UW Ob/Gyn physicians. The goal remains a commitment to bridge the gap between clinical and research training to enable young physicians to establish research careers and become independent investigators. Proposed training is a mentored experience with a successful investigator for a minimum of 2+ years. During this period, the scholar devotes most of her/his time to a research project(s) whereby he/she acquires the knowledge and skills to become independent and assume a faculty position. The UW Research Career Development Center has seventeen mentors with extensive research experience and funding who collectively represent both clinical /basic science expertise in subject areas that directly relate to women's health. This is a multidisciplinary proposal. Mentors have primary appointments at UW Ob/Gyn, Pediatrics, Medicine, Pathology, Molecular Biotechnology, Genetics, Physiology/Biophysics, and Psychiatry and Behavioral Sciences. The Department has a large pool of residents, fellows and junior faculty eager to compete for four proposed annual scholar awards. The Department and the School of Medicine at the UW are prepared to make major commitments of resources and funding to support this proposed research center.

Funding Source: National Institutes of Health (NIH)

Research

CYTOGENETICS

A Program of Research in Population Cytogenetics

Edith Y Cheng, MD, MS, Principal Investigator

Maternal meiosis I occurs during fetal ovarian development and describes a process by which pairs of chromosomes separate in an orderly fashion to provide daughter oocytes with an equal number of chromosomes. In order for chromosome pairs to separate and segregate normally, they must first pair and undergo genetic exchange. Abnormal conceptions result from the fertilization of chromosomally abnormal oocytes. Although we know the importance of these meiotic errors in the cause of human chromosome abnormalities (for example, Down syndrome), we know very little about the mediators and mechanisms by which chromosome pairs find and recognize each other, and exchange genetic material.

In this proposed study, we will examine how chromosomes find and associate with each other, using molecular cytogenetic techniques. Fluorescent *in situ* hybridization (FISH) using whole chromosome DNA will "paint the chromosomes of interest" and immunofluorescence technology for DNA-protein associations will potentially identify the mediators of these chromosome reactions. This approach has been successfully applied to male meiosis.

This study will be the first full scale analysis of the mechanisms involved in human female meiosis. Results of this study will provide answers to fundamental biological questions, including:
1) How does meiosis really happen?
2) Is the process different for males and females?
3) Is the process different for different chromosomes?

Funding Source: National Institutes of Health (NIH)

GYNECOLOGIC CANCERS

Clinical Implication of the Acquisition of BRCA1/2 Function in BRCA1/2-Deficient Ovarian Carcinoma

Elizabeth M Swisher, MD, Principal Investigator

Platinum compounds, such as cisplatin and carboplatin, are key drugs for the treatment of ovarian carcinoma. Both primary and acquired resistance to platinum compounds are serious clinical problems. The breast/ovarian cancer susceptibility genes BRCA1 and BRCA2 (BRCA1/2) play a critical role in repairing the DNA damage caused by platinum compounds. Consequently, BRCA1/2-deficient cells are hypersensitive to platinum compounds. Recently we found that platinum resistance of BRCA1/2-mutated cancer can be mediated by secondary intragenic mutations in BRCA1/2 that restore the wild-type BRCA1/2 reading frame. Based on this finding, we hypothesize that restoration of BRCA1/2 is involved in acquired platinum resistance of BRCA1/2-deficient ovarian carcinomas. In this proposal we focus on determining clinical relevance of restoration of BRCA1/2 function in BRCA1/2-deficient hereditary and sporadic ovarian carcinomas.

First, we will determine whether the occurrence of secondary mutations that restore DNA repair function of BRCA1/2 correlates with clinical outcome of primary and recurrent hereditary ovarian carcinomas occurring in women with inherited BRCA1/2 mutations. Second, we will evaluate whether restoration of BRCA1 expression is involved in the acquired resistance to platinum in sporadic ovarian carcinomas that initially have low BRCA1 expression before treatment. We will also determine whether ovarian cancer cells with reduced BRCA1 expression acquire restored BRCA1 function after in vitro selection in ther presence of cisplatin and evaluate regulatory mechanisms that lead to restored BRCA1 expression. With these studies we will assess the clinical significance of restoration of BRCA1/2 function in the treatment of BRCA1/2-deficient ovarian carcinoma

Funding Source: Fred Hutchinson Cancer Research Center (FHCRC)/NIH Flow Through

GYNECOLOGIC CANCERS

BRCA1/2 Restoration as a Predictor of Response in a GOG Clinical Trial for Recurrent Ovarian Carcinoma

Elizabeth M Swisher, MD, Principal Investigator

Most women with ovarian cancer have a good response to chemotherapy initially, but if the cancer comes back later, it is likely to become less responsive to chemotherapy. The resistant cancer grows unchecked and eventually kills the patient. We do not understand what makes many ovarian cancers resistant to chemotherapy. About 15% of ovarian cancers are caused by a familial risk, and we call these hereditary ovarian cancers. These cancers are usually caused by inherited mutations in the breast and ovarian susceptibility genes BRCA1 and BRCA2. Hereditary ovarian cancers are sensitive to chemotherapy because they lack functional BRCA1 or BRCA2.We discovered that hereditary ovarian cancers become resistant to chemotherapy by restoring BRCA1 and BRCA2, which allows the cancer cell to repair DNA damaged by chemotherapy. Many non-hereditary or sporadic ovarian cancers also start out deficient in BRCA1 and BRCA2. We think that restoration of BRCA1 and BRCA2 may be an important mediator of resistance to chemotherapy in both hereditary and sporadic ovarian cancers. We will test this idea by studying cancer tissues from women who are participating in a national clinical trial for the treatment of recurrent ovarian carcinoma. By using tissues and information from this clinical trial, we may develop a better predictor for whether a cancer will respond to a particular chemotherapy. By understanding what makes ovarian cancers resistant to chemotherapy, we may be able in the future to design better therapies for ovarian cancer and identify drugs that will make the cancer more sensitive to chemotherapy.

Funding Source: Mary Kay Ash Charitable Foundation

OCRF Symptom Study

Barbara A Goff, MD, Principal Investigator

Recent studies have shown that symptoms may be predictive of ovarian cancer. In April 2008 we began an NIH-funded (R21) pilot study to examine prospective screening of average-risk women for ovarian cancer in a primary care clinic setting using a symptom index followed by diagnostic testing using the CA125 blood test and transvaginal sonography (TVS) in index positive women. The goal of this pilot is to determine the feasibility of this multi-modal screening process and its acceptability to patients and clinic staff. We anticipate screening 3,000 women during this pilot effort. The proposed GCF/OCRF project would allow us to expand our pilot project, enrolling additional women and adding an additional clinical site, allowing us to screen a total of 13,000–15,000 women. the specific aims of this expanded pilot study would include determination of the percentage of women referred for further evaluation using the diagnostic tests because of a positive symptom index when the symptom index is used prospectively in a primary care clinic population over the age of 50; and estimation of the specificity of diagnostic testing using CA125 and TVS when used in a population of index positive women with symptoms potentially indicative of ovarian cancer. We anticipate identification of 500–600 women with a positive index score and 6–7 ovarian cancers, giving the expanded study the power to determine the rate of index positivity among average risk women over tp to within 1–2 percentage points, and to estimate the specificity of the multi-modal screening process as a whole.

Funding Source: Gynecologic Cancer Foundation

GYNECOLOGIC CANCERS

A Phase II Trial of Granulocyte-Macrophage Colony-Stimulating Factor (GN-CSF) with Weekly PROTEIN Bound Paclitaxel (Abraxane™) as Chemoimmunotherapy for First-Relapsed, Platinum-Resistant Epithelial Ovarian Cancer

Ron E Swensen, MD, Principal Investigator

Ovarian cancer is recognized by the immune system. Patients whose immune system recognizes ovarian cancer as "foreign" survive longer than patients whose immune system fails to reject the cancer. Dendritic cells process and present antigens to other immune cells in a way that either activates an immune response, if the antigen is identified as "foreign", or suppresses an immune response if the antigen is identified as "self. The "foreign" vs. "self" determination is made in dendritic cells when receptors of the innate arm of the immune system, that are preprogrammed to recognize foreign pathogens, are activated. Paclitaxel is commonly used to treat ovarian cancer, and is also capable of stimulating these innate system receptors, thus favorably affecting the immune system. GM-CSF is a cytokine that promotes the proliferation and maturation of dendritic cells, among other functions. GM-CSF alone has been shown to promote tumor regression in 38% of women with ovarian or breast cancer who were refractory to standard chemotherapy. Our clinical trial will give ovarian cancer patients paclitaxel, followed by GM-CSF. We also will measure immune system functions. We hypothesize that the paclitaxel will cause tumor cell death, thus releasing antigens for dendritic cells to scavenge. Paclitaxel will also stimulate the innate immune receptors on those dendritic cells. Subsequently, GM-CSF will stimulate the proliferation and maturation of dendritic cells. We hope that this combination of "chemoimmunotherapy" will stimulate the immune system to treat the invading tumor as "foreign" and promote immune rejection.

Funding Source: Berlex, Inc.

Research

GYNECOLOGIC CANCERS

Defining a Premalignant Phenotype in Fallopian Tube Epithelium (R01)

Elizabeth M Swisher, MD, Principal Investigator

The lack of an identifiable precursor lesion for ovarian carcinoma hinders attempts to design rational surveillance and chemoprevention for this deadly disease. Indeed, it is uncertain which are the specific cells in the female genital tract that transform into ovarian and primary peritoneal malignancies. A better understanding of the early steps in ovarian tumorigenesis would facilitate the development of new screening and prevention strategies. Women with a high risk of ovarian carcinoma may have early neoplasms identified at the time of preventive surgery, providing a rare glimpse of the earliest detectable disease. Inherited mutations in BRCA1 result in an ~40% lifetime risk of ovarian, tubal or peritoneal carcinoma. Current clinical recommendations for women with BRCA1 mutations include risk-reducing salpingo-oophorectomy (RRSO) by age 40 after completion of childbearing. Our group and others have identified a high rate of high-grade serous neoplasia in the Fallopian tubes of BRCA1 mutation carriers undergoing RRSO. The frequency of occult tubal neoplasia exceeds that of ovarian neoplasia when using a detailed surgical and pathological protocol. We hypothesize that most ovarian and peritoneal carcinomas arising in BRCA1 mutation carriers are seeded from neoplastic cells arising in the Fallopian tubes. This phenomenon could have important implications for the development of sporadic as well as hereditary ovarian carcinoma. The overall goal of the current proposal is to define a premalignant ovarian or tubal phenotype in women with inherited BRCA1 mutations.

The specific aims of this proposal are:

1) To characterize tubal epithelium in unaffected women with BRCA1 mutations and in women with BRCA1-associated or sporadic ovarian and peritoneal carcinomas
2) To identify priority genes that drive premalignant or early neoplastic alterations in pathologically normal tubal epithelium from women with BRCA1 mutations
3) To evaluate priority genes from Specific Aim 2 in inherited and sporadic ovarian and peritoneal carcinomas

Funding Source: National Institutes of Health (NIH)

Research

GYNECOLOGIC CANCERS

Falloposcopy: A Novel Approach to Ovarian Cancer Detection and Prevention

Elizabeth M Swisher, MD, Principal Investigator

Recent data suggest that many presumed ovarian or peritoneal carcinomas may actually arise in the Fallopian tubes. If true, then early detection of ovarian carcinoma should focus on viewing and sampling the Fallopian tube. Minimally invasive optical surveillance in the Fallopian tube is unavailable due to the lack of ultrathin and flexible endoscopic tools that provide high-quality imaging. The current technology which forms the basis for all flexible endoscopes has a severe trade-off of image quality with reduction of endoscope diameter when reaching the size of a single strand of spaghetti. A new technology has been developed at the University of Washington, providing high resolution (HDTV), small size and the flexibility needed to enter and transverse the Fallopian tube. Since the imaging uses low power laser light (essentially 3 laser pointers of red, green and blue), new spectroscopic capabilities for delineating between diseased, distressed and healthy tissue are now possible with or without fluorescence biomarkers. In future projects, a cell sampling tool will be used to remove cells from tissues of the Fallopian tube that appear suspicious for cancer or pre-cancer (neoplasia). The ability to sample cells under direct visualization at high optical resolution in the Fallopian tube could revolutionize early detection of ovarian cancer. This study will provide the pilot data from 8 women to demonstrate that Fallopian tube imaging in women at high risk for ovarian cancer is safe and effective and could be performed in an outpatient clinical setting. With our combined expertise in the molecular profiling of Fallopian tube in high-risk women and in the development of novel technologies for ultrathin endoscopy, our team is uniquely positioned to develop an entirely new approach for screening to prevent or treat early pelvic serous carcinoma.

Funding Source: Marsha Rivkin Center for Ovarian Cancer Research

GYNECOLOGIC CANCERS

The Fanconi Anemia-BRCA Pathway and Chemosensitivity of Human Cancer

Elizabeth M Swisher, MD, Principal Investigator

One of the most difficult problems in the treatment of cancer is acquired resistance to chemotherapy. Defects in DNA repair are likely to play a critical role in the sensitivity of cancer cells to chemotherapeutic drugs, many of which are DNA-damaging agents. Fanconi Anemia (FA) is a genetic disorder characterized by cancer susceptibility and cellular hypersensitivity to DNA crosslinking agents, such as cisplatin and melphalan. FA proteins and breast/ovarian cancer susceptibility gene products (BRCA1 and BRCA2) cooperate in a common DNA damage-activated signaling pathway (the FA-BRCA pathway), which controls DNA repair. We hypothesize that integrity of the FA-BRCA pathway is a critical determinant of resistance of tumor cells to chemotherapy with DNA crosslinking agents. The goals of our proposed research are
1) to elucidate the role of the FA-BRCA pathway in cisplatin sensitivity/resistance of cancer cells,
2) to determine if the sensitivity of tumor cells to DNA crosslinking agents can be increased by modulating the FA-BRCA pathway using small molecule inhibitors of the pathway, and
3) to further elucidate the mechanism of regulation of the FA-BRCA pathway.
We plan to determine the role of one of the FA genes, BRCA2/FANCD1, in acquired resistance to cisplatin using two BRCA2-deficient cell lines we recently identified.

Funding Source: Fred Hutchinson Cancer Research Center (FHCRC)

Identification of an Immunologic Signature of Ovarian Cancer for Use as an Early Cancer Screen

Heidi J Gray, MD, Principal Investigator

The goal of this proposal is to develop a serum-based assay that evaluates the use of antibody immunity as a diagnostic tool for early detection of ovarian cancer. There is ample evidence in the literature demonstrating the immunogenicity of ovarian cancer. Previous work has described several tumor-associated antigens and has shown patients have an ability to mount a T cell response to these antigens. It is well documented that evidence of exposure to tumor antigens exists by assaying for antibodies to tumor-associated antigens (TAAs). Evidence of this antibody response has been shown to occur early in tumorigenesis and therefore has potential for use as an early detection screen. The work proposed here will identify the immunologic signature of ovarian cancer composed of a panel of serum antibodies. The study will be done using serum samples from ovarian cancer patients and age-matched volunteer donors. The samples will be analyzed using a high-throughput technique that combines the use of a phage display library and protein array. This technique makes it possible to evaluate hundreds of phage-expressed proteins simultaneously to identify those that define the immunologic signature associated with ovarian cancer. The results of this study will provide data on the feasibility of multiparametric immune-based assays in discriminating patients with cancer from non-tumor bearing individuals and provide the basis for a definitive application validating the approach.

Funding Source: Ovarian Cancer Research Fund (OCRF)

Research

GYNECOLOGIC CANCERS

Premalignant Genetic and Epigenetic Alterations in Tubal Epithelium from Women with BRCA1 Mutations

Elizabeth M Swisher, MD, Principal Investigator

The overall goal of the current proposal is to identify genetic and epigenetic alterations in tubal epithelium from women with BRCA1 mutations that precede development of overt carcinoma. Approximately 10–15% of ovarian carcinomas occur secondary to inherited mutations in BRCA1 and BRCA2 which confer a 20–50% lifetime risk of ovarian carcinoma. This high risk, combined with the ineffectiveness of current screening methods, has led to the recommendation that women with mutations in BRCA1 and BRCA2 undergo risk-reducing salpingo-oophorectonmy (RRSO) by age 40 after completion of childbearing. A major obstacle in developing improved screening and prevention strategies is the lack of an identifiable premalignant neoplastic lesion that would facilitate study of the early events in malignant transformation.

Our group and others have identified a high rate of high grade serous neoplasia in the Fallopian tubes of BRCA1 mutation carriers undergoing RRSO. We hypothesize that many or most ovarian and peritoneal carcinomas arising in BRCA1 mutation carriers are seeded from neoplastic cells arising in the Fallopian tubes. This phenomenon could have important implications for the screening and prevention of hereditary ovarian carcinoma. BRCA1 is recognized to be important in chromatin remodeling. We have preliminary data that demonstrates our expertise at obtaining tubal or malignant epithelium by laser capture microdissection with RNA adequate for microarray expression analysis and DNA adequate for chromatin precipitation. We will combine analyses of epigenetic alternations with RNA expression studies to find molecular alterations in tubal epithelium in BRCA1 mutation carriers that are most likely to be functionally significant. Identification of precursor alterations and proof of their contribution to malignant progression would facilitate chemoprevention trials in high-risk women and provide new targets for early detection.

Funding Source: US Department of Defense (DOD)

HIV/AIDS

Effect of Lactobacillus on Genital HIV-1 RNA and DNA Shedding in Women

Jane E Hitti, MD, MPH, Principal Investigator

Genital HIV-1 viral load is a major predictor of sexual and perinatal HIV transmission, and strategies to decrease HIV-1 shedding, while promoting vaginal health, are urgently needed. We hypothesize that hydrogen peroxide-producing lactobacillus (*L. crispatus* and *L. jensenii*), key components of the normal vaginal flora, decrease genital HIV-1 RNA and DNA shedding among HIV-1-infected women by direct viral inhibition and also by relative suppression of potentially pathogenic vaginal bacteria associated with bacterial vaginosis (BV). We propose to evaluate this hypothesis using archived cervicovaginal lavage (CVL) and cervical cytobrush samples from parallel cohorts of HIV-1-infected women in the United States and Kenya. Specifically, we will: 1) Examine the effect over time of *L. crispatus, L. jensenii,* and *L. iners* presence and concentrations on HIV-1 RNA load in CVL, as well as the effect of these organisms on pro-inflammatory cytokines and other BV-associated flora. We anticipate that acquisition and/or higher concentrations of *L. crispatus* and *L. jensenii* (but not *L. iners*) will result in a significant decrease in CVL HIV-1 RNA, accounting for other factors such as plasma viral load and antiretroviral therapy, and that this protective effect may be mediated by down-regulation of pro-inflammatory cytokines and/or suppression of BV-associated bacteria; 2) Assess the longitudinal effect of vaginal Lactobacillus species, other BV-associated organisms, and pro-inflammatory cytokines on endocervical HIV-1 DNA quantitation, as well as endocervical HIV-1 RNA. We hypothesize that the protective effect of *L. crispatus* and L. *jensenii* will extend to the endocervix and will include a decrease in proliferation of HIV-1-infected cells as well as viral replication.

Taken together, these aims will add to our understanding of the mechanisms by which hydrogen peroxide-producing lactobacillus modulates HIV-1 in the female genital tract, and may add rationale for further evaluation of probiotics as a potential secondary HIV-1 prevention strategy.

Funding Source: National Institutes of Health (NIH)

HIV-Specific Antibodies in Vaginal Swabs from HIV-Uninfected HPTN-035 Participants

Florian Hladik, MD, PhD, Principal Investigator

HPTN 035 is a phase II/IIb safety and effectiveness study of the vaginal microbicides buffer gel and 0.5% PRO 2000/5 gel for the prevention of HIV infection in women. This study will address the hypothesis that women sexually exposed to HIV-1 (while using a topical microbicide) and who remain uninfected develop a compartmentalized humoral immune response. Secretions extracted from vaginal swabs will be tested for HIV-specific IgG and IgA antibodies by luminex technology. These assays will be performed in collaboration with Dr. Georgia Tomaras (Duke University, NC). We will initially screen swabs from 100 HIV-uninfected and 10 HIV-infected women (positive controls). The luminex technology enables multiplexed quantification of both IgG and IgA antibodies directed at HIV-1 clade C consensus sequence antigens, including Env gp120, Env gp41, Gag and accessory proteins. Based on the initial results with 100 HIV-uninfected women, we will continue to screen a larger cohort of HPTN 035 participants.

Funding Source: Magee-Womens Research Institute and Foundation

Research

HIV/AIDS

UW IMPAACT Clinical Trial Unit

Jane E Hitti, MD, MPH, Principal Investigator

The Seattle Children's Hospital/University of Washington International Maternal, Pediatric and Adolescent AIDS Clinical Trials (IMPAACT) site is the only perinatal/pediatric clinical trials unit in the Pacific Northwest, and offers treatment trials to all HIV-infected pregnant women and HIV-exposed or infected children in the region. These funds support the screening, enrollment, and follow-up of HIV-infected pregnant and postpartum women and their HIV-exposed infants into clinical trials in the IMPAACT network, with attention to providing excellent quality of data collection and timeliness.

Funding Source: Seattle Children's Hospital/Research

Comparison of Immune Cells in the Cervix Between Women With and Without Detectable Genital HIV-1

Caroline M Mitchell, MD, MPH, Principal Investigator

Over 15 million women are infected with HIV-1 worldwide, primarily through heterosexual intercourse. Transmission of HIV-1 to the male sexual partners for infants at the time of delivery occurs through shedding of HIV-1 in the cervicovaginal secretions. Some HIV-1 infected women have high levels of vaginal HIV-1 shedding, while others have no detectable virus. Epidemiologic studies suggest that while plasma viral load is an important predictor of genital shedding of HIV-1, genital tract infections and local inflammation may also promote viral shedding. However, the mechanism for this association has not been described, and interventions to treat infections have not always decreased genital shedding of HIV-1. We hypothesize that trafficking of infected cell to the genital tract and proliferation of HIV-1 infected CD4+ T cells in the genital mucosa are an important determination of HIV-1 genital tract shedding. Our studies have shown that genital tract virus is composed of many identical genetic sequences (i.e., monophyletic), which suggests proliferation of infected cells that are either resistant cells or traffic to the genital tract. In this study we aim to test out hypothesis in two ways:

1) To compare the number of CD4+ T cells in cervical biopsy sections between women with and without genital HIV-1 shedding, and
2) To compare the number of CD4+ T cells in cervical biopsy sections between women with and without monophyletic viral sequences

Funding Source: Puget Sound Partners for Global Health (PSPGH)/
Fred Hutchinson Cancer Research Center (FHCRC)

Research

HIV/AIDS

The Role of Exosomes in Semen for HIV Infection of the Genital Mucosa in Women

Florian Hladik, MD, PhD, Principal Investigator

The goal of this project is to investigate how small subcellular particles in semen, seminal exosomes, impact the heterosexual transmission of HIV to women and the induction of genital anti-HIV immunity

Funding Source: University of Washington (Royalty Research Grant)

Standardization and Comparative Assessment of Mucosal Sampling Techniques for Evaluating Vaccine-Induced Immune Responses

Florian Hladik, MD, PhD, Principal Investigator

This study is a collaborative effort between five independent laboratories (Seattle, Chicago, Nairobi, Cape Town and Antwerp) to optimize and standardize sampling of mucosal specimens from the female genital tract for the measurement of HIV vaccine-specific immune responses.

Funding Source: NIH/NIAID via HVTN

Mucosal Anti-HIV Antibodies in Exposed Uninfected Women Participating in Microbicide Trials

Florian Hladik, MD, PhD, Principal Investigator

This goal of this project, which will be carried out in collaboration with Dr. Georgia Tomaras (Duke University), is to determine if HIV-1 exposed uninfected women participating in microbicide trials have measureable anti-HIV antibodies in vaginal swab specimens. Such a compartmentalized humoral immune response could potentially contribute to protection of these women against HIV infection.

Funding Source: Bill and Melinda Gates Foundation

Leadership Network Application, Priority Area Microbicides

Florian Hladik, MD, PhD, Co-Principal Investigator, Immunology Core

The mission of the MTN is to reduce the sexual transmission of HIV through the development and evaluation of products, which reduce the transmission of HIV when applied topically to mucosal surfaces. The goal is to conduct scientifically rigorous and ethically sound clinical trials of microbicide safety and effectiveness, which will support licensure of these products.

Funding Source: NIH/NIAID

Research

MENOPAUSE

EQUOL and Vasomotor Symptoms

Susan D Reed, MD, MPH, Principal Investigator

Soy foods contain two isoflavones, genestein and daidzein, that act as either estrogen agonists or estrogen antagonists, depending on the estrogen receptor location. Several intervention studies have evaluated the effects of soy isoflavones on menopausal symptoms, particularly vasomotor symptoms. However, these studies have yielded inconsistent results. Daidzein is metabolized in the lower segment of the digestive system by intestinal flora, to yield equol (an active metabolite). Equol's physiological activity has been receiving close attention, since the potential to bind to estrogen receptors (ERs), particularly ER-beta, is higher with equol than with soy isoflavone itself. Equol formed by intestinal flora is absorbed and eliminated into urine. Findings of another recent study suggest that menopausal symptoms are associated more closely with equol than with daidzein or genistein ingested directly from foods. Furthermore, in this same study, the percentage of women capable of eliminating equol into urine was low for women with more severe menopausal symptoms, suggesting that the presence/absence of equol formation in the intestine is closely related to the severity of menopausal symptoms We are specifically interested in the interplay between ingestion of soy foods, equol producer status, and vasomotor symptoms in midlife women. In the wake of the Women's Health Initiaitive, use of hormone therapy for vasomotor symptoms decreased dramatically, and women are seeking safe alternatives for symptom management. The proposed study is a first step in evaluating the interplay between soy food metabolism and relief of VMS, with the ultimate goal of determining whether more specific treatment with equol may relieve VMS in subsets of women. Our specific aims are:

1) To investigate the prevalence of soy food consumption and associated prevalence of vasomotor symptoms in healthy midlife US women in the Seattle area not using hormone therapy
2) Among a subset of women identified with adequate soy intake, evaluate urinary isoflavonoid excretion and relation to objective and subjective frequency of vasomotor symptoms and subjective severity and bother

Funding Source: Group Health Center for Health Studies

Research

MENOPAUSE

MSI-FLASH: An RCT of Yoga and Ultra Low-Dose Estrogen Gel for Vasomotor Symptoms (R01)

Susan D Reed, MD, MPH, Principal Investigator

This application describes one of five proposals being submitted in conjunction with the network application entitled "The Menopausal Symptoms Initiative—Finding Lasting Answers to Sweats and Hot Flashes (MSI-FLASH)". Our network and data coordinating center will be jointly led by two Co-Principal Investigators of the Women's Health Initiative, Clinical Coordinating Center (Seattle) who have worked together for over a decade (LaCroix, Anderson, PIs). The MSI-FLASH network has five clinical sites located in Boston, MA (Cohen, Joffe, PIs), Indianapolis, IN (Carpenter, PI), Oakland, CA (Sternfeld, Caan, PIs), Philadelphia, PA (Freeman, PI) and Seattle, WA (Newton, Reed, PIs). This multidisciplinary investigator group proposes five randomized controlled trials testing a range of behavioral, mind-body, hormonal and pharmacologic interventions. Our aims are to fulfill the main objective of the RFA, "New Interventions for Menopausal Symptoms (U01)", and to accelerate the identification of effective remedies for vasomotor symptoms (VMS). In this site application we propose a multicenter RCT of yoga and ultra low-dose estradiol (E2) gel and placebo gel to be conducted in Seattle, Indianapolis and Boston.

The primary aims of this RCT are to evaluate the effects of yoga alone and ultra low-dose E2 gel alone vs. placebo gel on:
1) subjective VMS frequency, and
2) VMS bothersomeness

Secondary aims are:
1) to evaluate the effects of yoga alone and ultra low-dose E2 gel alone on objective VMS frequency, sleep and mood, and
2) to examine whether the combined effect of yoga and ultra low-dose E2 is greater than the effects of either alone on the above outcomes (this aim will only be explored if yoga alone affects at least one of these outcomes).

Hypotheses:
1) Yoga will improve subjective VMS more than placebo gel
2) Yoga will improve VMS bothersomeness more than placebo gel
3) Ultra low-dose E2 gel will improve subjective VMS more than placebo gel, and
4) Ultra low-dose E2 gel will improve symptom bothersomeness more than placebo gel

To accomplish our specific aims we will:
1) recruit and randomize 400 women to one of four treatment arms for 12 weeks—placebo gel, yoga + placebo gel, ultra low-dose E2 gel, or yoga + ultra low-dose E2 gel
2) measure above outcomes at baseline and 23 weeks, and
3) compare changes in outcomes in yoga and ultra low-dose E2 gel groups to placebo gel

Funding Source: National Institutes of Health (NIH)

Research

MUCOSAL IMMUNOLOGY

The Female Genital Innate Immune Response to Vaginal Microbiota (K08)

Caroline M Mitchell, MD, MPH, Principal Investigator

Bacterial vaginosis (BV) is a vaginal syndrome characterized by an overgrowth of anaerobic vaginal bacteria, and is associated with several adverse clinical outcomes, including pelvic inflammatory disease, preterm birth and increased risk of HIV-1 acquisition. The individual bacterial species differ between individuals, as do the clinical symptoms, incidence of serious sequelae, and patterns of cytokine response. We hypothesize that clinical differences result from the interactions between individual species and host immune responses. We plan to test the following hypotheses:|

1) some bacterial species downregulate innate host responses, allowing high levels of colonization by decreasing levels of vaginal cytokines and/or production of antimicrobial peptides (beta-defensins, cathelicidin, secretory leukocyte protease inhibitors (SLPI), lactoferrin)
2) some individuals are more vulnerable to colonization due to low baseline levels of those antimicrobial peptides
3) Lactobacillus species and BV-associated pathogens activate the innate immune response differently via pattern-recognition receptors like TLR-2, and
4) some bacterial species are more likely to colonize the upper genital tract due to the presence of virulence factors or mechanisms for subverting the host immune response

We will characterize prospectively collected daily vaginal swabs from 30 women for levels of individual bacterial species using qPCR for the 16S rRNA gene, and correlate these with the temporal response in levels of cytokines and antimicrobial peptides (Aim 1). Responses in vaginal epithelial cell culture will be used to determine whether lactobacilli and BV-associated microbes activate toll-like receptors differently resulting in different cytokine profiles, and whether TLR-2 activation is associated with higher levels of antimicrobial peptides (Aim 2). Endometrial samples collected at hysterectomy will be characterized by broad range 16S rRNA PCR and pyrosequencing to detect upper genital tract colonization and define the microbiota in comparison to vaginal mirobiota in the same women. In addition, levels of cervical cytokines and defense molecules will be measured to assess their relationship with upper tract colonization (Aim 3).

The PI for this application, Caroline Mitchell, MD, MPH, is an Ob/Gyn whose goal is to understand how the female genital tract defends against bacterial pathogens, with the ultimate endpoint of developing better therapeutic and preventive interventions. Her mentor, Dr. David Fredricks, is a nationally recognized investigator known for using advanced molecular techniques to better characterize the vaginal microbiota, and has recently been recognized for excellence in mentoring. The University of Washington is the top public university for research funding, with an internationally renowned Infectious Diseases program and a long history of studies on BV. The scientific advisory committee has expertise in immunologic techniques, clinical trials and data analysis.

Funding Source: National Institutes of Health (NIH)

Research

NEUROENDOCRINE

Neurochemical and Neuroendocrine Function during Aging

Phyllis M Wise, PhD, Principal Investigator

The brain plays a critical role in the transition to reproductive senescence. The virtual lack of ovarian estrogens during the postmenopausal period in women clearly impacts multiple aspects of brain function. We have found that during middle age, the ability of estradiol to modulate the neurochemical events that are required for preovulatory GnRH/LH surges diminishes. The ability of the suprachiasmatic nucleus, the major circadian pacemaker in mammals, to drive diurnal neurochemical events declines, which leads to imprecision in the timing of the GnRH/LH surge.

Estradiol exerts important non-reproductive actions that protect the brain against neurodegenerative conditions. Therefore, its absence during postmenopause leads to increased vulnerability to injury and diseases of the brain. We will test three working hypotheses:

1) During middle age, attenuation in the diurnal rhythmicity of VIP and/or GABA or responsiveness of GnRH neurons to these neurotransmitters influences the synthesis, activation and/or secretion of GnRH
2) The presence or absence of estradiol influences the interactions of these neurotransmitters with GnRH
3) Estradiol is critical for maintaining normal brain function and for protecting against neurodegeneration associated with disease or injury

Our results will provide new insights into the cellular and molecular basis of brain aging. They will deepen our understanding of how estradiol modulates the process of brain aging and how its absence impacts brain function. This information is critical in developing new strategies to treat women as they approach the perimenopausal and postmenopausal periods.

Funding Source: National Institute on Aging (NIA)

Research

NEUROENDOCRINE

Kisspeptin-GPR54 in the Female Neuroendocrine Axis

Robert A Steiner, PhD, Principal Investigator, and Donald K Clifton, PhD, Co-Investigator

Neurons in the hypothalamus that produce gonadotropin-releasing hormone (GnRH) are the pathway by which the brain coordinates reproductive cycles in female mammals. The overall goal of this research is to identify the neural circuits and molecular mechanisms that regulate the secretion of GnRH, focusing specifically on how KiSS-1 neurons directly control GnRH neurons. KiSS-1 neurons in the arcuate nucleus (ARC) and anteroventral and periventricular nucleus (AVPV) of the hypothalamus are direct targets for the negative and positive feedback action of the ovarian hormone estradiol (E2) on GnRH secretion. However, the ovary produces additional hormones, besides E2, that are vital for regulating reproduction, including progesterone (P), which plays an important role in brain development, ovulation and pregnancy in women. The specific aims of this proposal are focused on learning how P and its receptor (PR) control the activity of KiSS-1 neurons and thus regulate GnRH secretion and coordinate reproductive function in females. The basic approach to this problem involves the use of ovariectomized rats and mice (wildtype and transgenic) and analysis of the effects treatments of E2 and P, as well as specific agonists and antagonists, have on the molecular physiology of the brain. The effects of these hormonal manipulations will be assessed through the use of *in situ* hybridization to measure cellular expression of the genes coding for key neurotransmitters, relevant receptors, and indicators of cellular activation in KiSS-1 neurons (e.g., Fos induction), as well as radioimmunoassays to measure circulating levels of gonadotropins (LH and FSH) and ovarian hormones. Specifically, the experiments are designed to: 1) investigate the effects of P on KiSS-1, Dyn (dynorphin), and NKB (neurokinin B) gene expression in KiSS-1 neurons in the ARC; 2) determine whether KiSS-1 neurons express PR and whether the expression of PR is induced by E2; 3) evaluate the legend-dependent and -independent role of PR in KiSS-1 neurons in the ARC and AVPV; and 4) ascertain whether P acts in a time-dependent manner to either stimulate or inhibit the activity of KiSS-1 neurons involved in positive feedback (in the AVPV). Understanding the cellular and molecular basis of PR signaling in the brain is a necessary step towards a more thorough understanding of reproductive physiology. Progestins (drugs that are similar to P) are widely used as contraceptive agents. Moreover, P itself is used early in pregnancy to prevent miscarriage and later in pregnancy to forestall preterm births. Nonetheless, there is a significant gap in our understanding of P action in the brain and a virtual void in what is known about PR signaling in KiSS-1 neurons. The studies outlined in this proposal are designed to advance our fundamental knowledge of reproductive neuroendocrinology—to enable women and their families to overcome problems related to infertility, to understand the benefits and risks of hormonal therapies, and to provide an empirical foundation for the development of new and better strategies to treat reproductive disorders and offer improved methods of contraception.

Funding Source: National Institutes of Health (NIH)

Research

NEUROENDOCRINE

Project II—Kiss1 Signaling and Regulation in the Male Mouse (U54)

Robert A Steiner, PhD, Principal Investigator, and Donald K Clifton, PhD, Co-Investigator for Project II (G. Stanley McKnight, PhD, Principal Investigator for overall grant)

The overarching goal of this project is to understand the physiological function of kisspeptin signaling in neuroendocrine control of reproduction in the male. In humans, loss of function mutations in genes encoding either kisspeptin (Kiss1) or the kisspeptin receptor (Kiss1r or GPR54) cause a failure of puberty and infertility. Kiss1-expressing neurons in the brain are found in the arcuate nucelus of the hypothalamus (ARC), where they directly control secretion of gonadotropin-releasing hormone (GnRH), which is the final common pathway through which the brain regulates reproduction. In the male, Kiss1 neurons act as central processors of reproduction, serving as a cellular conduit linking testosterone (T) secretion from the testes and GnRH release from the brain. Kiss1 neurons in the ARC have a unique property—they co-express neurokinin B (NKB) and dynorphin (Dyn), which, together with kisspeptin, control GnRH secretion. The expression of NKB in those neurons is especially significant, as disruptive mutations of the genes that encode NKB and its receptor in humans (TAC3 and TAC3R) result in reproductive failure. Yet despite their obvious importance, Kiss1 neurons remain a fundamental mystery; we have no clear understanding of the cellular and molecular mechanisms that govern their activity, much less the specific functions of the neurotransmitters, NKB and Dyn. The specific aims of this proposal are to identify the mechanisms by which T regulates the activity of Kiss1/NKB/Dyn neurons in the brain. The experimental approach involves the use of novel Cre-eGFP technology to target Kiss1 neurons, map and manipulate their transcriptome, study the physiological implications of altering their activity, investigate their boiophysical properties, and analyze their functional significance by inductive reasoning.

Funding Source: National Institutes of Health (NIH)

Research

PREECLAMPSIA

Maternal-Fetal Immune Tolerance in Preeclampsia

Hilary S Gammill, MD, Principal Investigator

We hypothesize that inadequate immunologic tolerance of the fetus by the mother contributes to the development of preeclampsia. Several lines of evidence point toward an immunologic contribution to the pathophysiology of preeclampsia. In normal pregnancy, general maternal immunocompetence in the face of specific tolerance of the semiallogeneic fetus suggests tolerance mechanisms that are antigen-specific. Quantitative and qualitative changes in regulatory T cells play an important role in adaptation to normal pregnancy. Early studies show heightened maternal cellular reactivity against fetal cells in preeclampsia as compared with normal pregnancy, but the precise mechanisms and cellular populations involved have not been elucidated. The proposed studies will launch novel mechanistic investigations aimed to begin to understand immunopathogenic contributions to preeclampsia. If aberrant regulatory mechanisms are confirmed, this area presents an important point of potential therapeutic intervention, an area which is already under active investigation in the areas of transplantation and autoimmunity.

Funding Source: Preeclampsia Foundation

Maternal-Fetal Immune Tolerance in Preeclampsia

Thomas J Benedetti, MD, MHA, Principal Investigator

This project is primarily intended to address the March of Dimes' funding priority:

a) Increasing risk reduction education and/or services in women at high risk due to previous adverse pregnancy outcomes in which pre/interconception or prenatal care could help prevent adverse outcomes and funding priority
b) Increasing professional education about 17α-hydroxyprogesterone caproate treatment for women who had a previous singleton preterm infant

History of a previous preterm birth is a primary factor prior to preganancy that identifies women at substantial risk for recurrent preterm birth and is present in 10% of all women delivering preterm. These women have at least a 3X higher risk of preterm birth in a subsequent pregnancy, with rates ranging from a low of 25% to a high of 55%, depending primarily on ethnicity, number of previous preterm births, and interpregnancy interval. In this 3-year demonstration project we will provide enhanced preconception care to women who have delivered a preterm infant. We propose to conceptually expand the preconception time to begin immediately after birth and to include the first six weeks of the postpartum period, times we have found to be teachable moments for patients having suffered the experience of a preterm birth. We will develop and provide both in-hospital and outpatient education materials to patients regarding strategies with a high likelihood of reducing their risk of recurrent preterm birth: reliable contraception for at least one year, 17-OH progesterone, and counseling about smoking cessation, dental hygiene, and stress reduction. We will coordinate and share outpatient educational activities with the patient's primary care obstetric provider. We will assess patient satisfaction with these educational interventions and follow the patients at 6-month intervals to evaluate behavior modification and subsequent pregnancy outcome.

Funding Source: March of Dimes, Washington Chapter

Research

PRETERM BIRTH

New Model of Ascending Infection-Related Preterm Birth

Kristina M Adams Waldorf, MD, and Michael G Gravett, MD, Co-Investigators

Preterm birth remains a significant economic and public health burden and the incidence is rising. Infection-induced inflammation plays a significant role in preterm birth and is thought to occur as a result of either direct microbial infection or microbial byproduct stimulation of inflammatory mediators, which promotes premature myometrial responses and uterine contractions. Intra-amniotic infection is thought to be the result of ascending bacterial infection from the vagina, and immune responses to bacteria are thought to drive preterm labor and promote fetal acute brain and lung injury.

Obstetrical research has yet to identify effective preventive interventions for preterm labor. The overall objective of this proposal is to develop a model system which emulates human preterm birth to ultimately elucidate molecular mechanisms of infection-induced preterm labor and related adverse neonatal sequelae (e.g., brain injury). We propose to develop a non-human primate model in the rhesus monkey that closely mimics an ascending lower genital tract infection at the chorio-decidual interface in the lower uterine segment. This model could provide important mechanistic observations that cannot be determined in lower mammalian models of preterm birth, due to known differences in placentation and parturition (onset of labor).

The central hypothesis is that infection with Group B streptococcus (GBS) at the chorio-decidual interface in the lower uterine segment will result in an inflammatory response that stimulates premature myometrial contractions, intra-amniotic infection, and premature delivery. We propose to establish a model of preterm labor that more closely replicates the natural history of human preterm labor than prior animal models, by mimicking an ascending lower genital tract infection in a rhesus monkey. The new model will introduce GBS at the chorio-decidual interface in the lower uterine segments of a pregnant dam, monitor maternal and fetal physiological responses before and during infection, and sequentially sample the maternal, fetal and amniotic fluid compartments.

We believe these initial experiments will lay the foundation for our longer term objectives which are:
1) to elucidate the pathophysiologic mechanisms of ascending infection-induced preterm labor
2) to establish the cellular and molecular links in intrauterine infection and preterm labor using genomics
3) to develop non-invasive diagnostic strategies for detecting infection-associated preterm labor

Funding Source: March of Dimes

Research

PRETERM BIRTH

Toll-Like Receptor Antagonism as a Potential Treatment for Preterm Labor (K08)

Kristina M Adams Waldorf, MD, Principal Investigator

The overall goal of my Career Development Award is to become an independent investigator of immune responses in a chronically-catheterized non-human primate model of infection-induced preterm birth. There are four objective of my training plan:
1) Develop skills in working with the chronically-catheterized non-human primate
2) Gain greater experience in the investigation of reproductive immunology and host-pathogen interactions
3) Master basic and advanced elements of biostatistics and study design
4) Acquire practical skills necessary for an academic research career

The chronically-catheterized non-human primate model allows serial sampling of the maternal, fetal, and amniotic fluid compartments. After experimental infection of the amniotic fluid, maternal and fetal immune and endocrine responses can be correlated with uterine contractility and fetal histopathology. The main objective of the research plan is to determine whether the innate immune response to intrauterine infection is a critical event in the pathogenesis of infection-induced preterm labor and fetal lung injury.

Funding Source: National Institutes of Health (NIH)

Non-Human Primate Model of Stretch-Induced Preterm Labor

Kristina M Adams Waldorf, MD, Principal Investigator

Preterm birth remains a significant economic and public health burden and the incidence is rising. Our objective is to develop a non-human primate model of stretch-induced preterm labor (PTL) to elucidate the mechanisms involved and to test novel therapies. Uterine stretch is often responsible for the onset of PTL in multiple gestation, which accounts for 15% of preterm births and 50% of the increase in preterm birth rates over the last decade. Women with a multiple gestation can be identified by early ultrasound, making them an ideal group to target for prophylactic interventions. The unifying hypothesis is that a novel non-human primate model of uterine stretch will emulate human stretch-induced PTL and define the initiating and subsequent events in the pathogenesis of this type of PTL. Previously, we have defined intracellular mechanisms responsible for stretch-induced expression of labor-associated genes *in vitro* and now need to establish an animal model in which to test potential therapeutic intervention. We will take advantage of a well-established, chronically-catheterized, non-human primate model to create stretch-induced PTL by inflating an intra-amniotic balloon. Our non-human primate model is superior to lower mammalian models of PTL since it shares many features with human pregnancy, including placental structure and hormonal control of parturition. This model will allow sequential sampling of myometrium, maternal, and amniotic fluid compartments before and after uterine stretch. If interventions to prevent PTL in multiple gestations are to be achieved, then pathways activated by uterine stretch must be elucidated in a model that emulates the human condition.

Funding Source: March of Dimes Birth Defects Foundation

TOPICAL MICROBICIDE DEVELOPMENT

Improved Macaque Safety Model for Topical Microbicides: Post-Coital Assessments

Dorothy L Patton, PhD, Principal Investigator

Topical microbicides represent an emerging strategy for the prevention of transmission of HIV and other sexually transmitted infections. A successful topical microbicide product could be applied prior to intercourse, and would have activity against a variety of STIs, including HIV. It will be acceptable to potential users in terms of physical characteristics, availability, ease of use, safety and efficacy properties. We have utilized a macaque vaginal safety model to provide standardized preclinical safety data for numerous topical microbicide products in development. In this model, measures of product safety include cervicovaginal colposcopy, vaginal microbiologic evaluation and vaginal pH monitoring. This model characterizes the vaginal environment's response to repeated topical product applications in the absence of the exogenous factors of intercourse and potentially infectious ejaculate. We have yet to investigate the effects of sexual intercourse on the cervicovaginal environment. Mucosal perturbation and potential micro-trauma in the form of epithelial abrasions are likely to result from sexual activity. Additionally, the effects that seminal fluid may induce on the cervicovaginal environment, as well as semen's effects on topical microbicide product safety and efficacy, have not yet received their due attention. It is imperative that these factors be assessed, as they may have significant impact on a topical microbicide's acceptability and efficacy. We propose to enhance our standardized vaginal safety evaluations conducted in the pigtailed macaque model to include evaluations after sexual activity and with the presence of seminal fluid.

Funding Source: National Institute of Allergy and Infectious Diseases (NIAID)

Topical Microbicide Safety Testing in Macaques

Dorothy L Patton, PhD, Principal Investigator

Research efforts to develop topical microbicides for intravaginal use in the prevention of sexually transmitted infections, including HIV, have been ongoing for nearly a decade. An estimated 333 million new cases of vaginally and rectally transmitted diseases occur in the world each year according to the World Health Organization. Clearly, an ideal microbicide would prevent the transmission of both vaginally and rectally acquired sexually transmitted infections (STI). Therefore, topical miocobicide products must be tested to ensure that the sexual transmission of HIV and other sexually transmitted infections is prevented, and that the vaginal and rectal environments are preserved. We have developed useful models to evaluate the safety of topical microbicide products after vaginal and rectal use in the pigtailed macaque. We have used these models to study the effects of single and repeated applications of microbicides on vaginal and rectal microflora and epithelium. One of the strengths of the macaque model is the similar vaginal and rectal microflora shared by the pigtailed macque and humans. The presence of endogenous lactobacilli, and of H_2O_2-producing lactobacilli in particular, provides for studies which determine a product's influence on vaginal micobiology and, more importantly, on the production of H_2O_2 in the vaginal milieu, which is known to have antimicrobial properties.

Funding Source: University of Central Florida/Flow Through from NIH

Research

TOPICAL MICROBICIDE DEVELOPMENT

Project 2— Nonhuman Primate Studies of Tenofovir and UC781 (of Alternative Formulations of Tenofovir and UC78)

Dorothy L Patton, PhD, Principal Investigator for Project 2
(Sharon Hillier, PhD, Principal Investigator for overall grant)

We have developed a useful model to evaluate the safety of topical microbicide products after vaginal use in the pigtailed macaque. We have used this model to study the effects of single and repeated applications of microbicides on vaginal microflora and epithelium. We have conducted preclinical safety and pharmacokinetic studies of vaginal gel formulations containing UC781 (1% and 0.1%) and tenofovir (1%) in this macaque model. In addition, we have the ability to image (MRI) product dispersal and transport in the female reproductive tract.

In this proposed cooperative agreement, a novel delivery system for topical microbicides, vaginal films, will be compared to vaginal gel formulations. We will use our macaque model to assess safety, dispersal and pharmacokinetic characteristics of various film formulations containing UC781 and/or tenofovir, and compare these findings to those compiled for gel formulations. Finally, we will assess the efficacy of each of the developed film products using a macaque model for RT-SHIV infection. These studies will in part guide the optimization of a combination topical microbicide delivery system.

Funding Source: National Institutes of Health (NIH)

Research

VACCINE DEVELOPMENT

Safety and Efficacy of Chlamydia Vaccine Candidates

Dorothy L Patton, PhD, Principal Investigator

A Randomized, International, Double-Blind, Controlled with GARDASIL TM, Dose-Ranging, Tolerability, Immunogenicity, and Efficacy Study of a Second Generation Human Papillomavirus L1 Virus-Like Particle Vaccine Administered to 16 to 26 Year Old Women

Constance Mao, MD, Principal Investigator