

WINTER 2008



STANFORD Women's Health magazine

Cardiovascular Health... Does Sex/Gender Matter?

ALSO IN THIS ISSUE

Who is Winning (at Losing Weight)?
Changes in Female Sexual Function...
Throughout the Lifespan

New Specialized Care for Pediatric
and Adolescent Girls

Breast Cancer Gene Mutation
Study Findings



*From left to right: Hannah Valentine, MD;
Marcia Stefanick, PhD; and Lynn Westphal, MD*

STANFORD Women's Health magazine



Welcome to Women's Health Magazine!



Lynn Westphal, MD



Jim Batterson

We are pleased to publish our inaugural issue of Women's Health Magazine and begin sharing with you, Stanford University Medical Center's commitment to women's health.

In the landmark 2001 Institute of Medicine report, *Exploring the Biological Contributions to Human Health: Does Sex Matter?*, those in the medical field were alerted to the previously overlooked role of sex/gender in the physiology of disease and to the enormous potential for improving medical care to women. The interest in sex-based biology was heightened and a new, more interdisciplinary, integrated view of women's health became the prevailing paradigm.

Also in 2001, Women's Health at Stanford, as envisioned by Linda Giudice, MD, PhD and embraced by School of Medicine Deans Bauer and Pizzo, was launched. The program blended biomedical and social science together in a way to encourage more comprehensive, multidisciplinary, sex-based research, education and clinical care. The Women's Health program (as it is now known) continues to act as a supporter and facilitator of the great efforts being made by so many talented medical professionals at Stanford.

Our first issue begins an ongoing effort to share news about the various people and programs that are enhancing the health of women here at Stanford, and by way of their discoveries, throughout the world. Special attention is given in this issue to the Women's Heart Health at Stanford program; our Women's Health mentoring programs; and the distinctive, multidisciplinary Female Sexual Medicine program. Other articles discuss recent developments and discoveries in breast cancer research; the launch of the Human Immune Monitoring Center, and our new Pediatric and Adolescent Gynecology program. Future issues will feature pregnancy and motherhood (May) and women and cancer (September).

There are many colleagues and friends we thank for making this magazine possible – too many to mention in this short space and ensure everyone meriting such gratitude is recognized. We do, however, wish to pay tribute to the School of Medicine's Office of Communications & Public Affairs; the Informational Resources and Technologies group; and Stanford's Visual Arts Services; for contributing materials and expertise. We particularly want to thank Betty and Bob Joss, who contributed vision, encouragement and funding support to ensure that the public is made aware of the world-class medical research, education and clinical care being brought to women by the Stanford University Medical Center. We extend our deepest appreciation to Betty and Bob for making this publication a reality.

Sincerely,

Lynn Westphal, MD
Director
Women's Health

Jim Batterson
Executive Director
Women's Health

inside this issue

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Highly specialized, expert care is a hallmark of the SUMC. See how a new clinic brings such targeted medical services to pediatric and adolescent girls.

10 **Cover Story** Women's Heart Health at Stanford Program

An examination of one of the Cardiovascular Institute's top priorities, the Women's Heart Health at Stanford program, as the nation celebrates the American Heart Association's heart health month (February) and its ongoing "Go Red for Women" campaign.

18 Female Sexual Medicine

Almost half of all women experience sexual dysfunction, yet do not know where to turn for medical care. Stanford's Leah Millheiser, MD addresses that void by developing one of the country's top programs in female sexual medicine.

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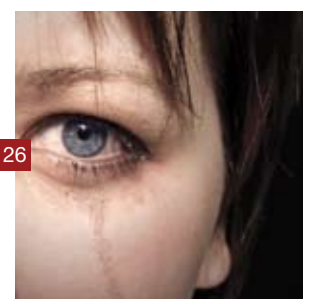
Many autoimmune diseases afflict women at much higher rates than men. See how this new Stanford center is accelerating immune system research.

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what is women's health?

On September 26, 1994, the National Academy on Women's Health Medical Education adopted the following definition of "women's health"... which became the prevailing reference for future investigative and clinical care efforts ...

Women's health is devoted to facilitating the

- preservation of wellness and
- prevention of illness in women,

And includes screening, diagnosis, and management of conditions which

- are unique to women
- are more common in women
- are more serious in women
- have manifestations, risk factors, or interventions which are different in women.

It also

- recognizes the importance of the study of gender differences
- recognizes multidisciplinary team approaches
- includes the values and knowledge of women and their own experience of health and illness
- recognizes the diversity of women's health needs over the life cycle, and how these needs reflect differences in race, class, ethnicity, culture, sexual preference, and levels of education and access to medical care
- includes the empowerment of women, as for all patients, to be informed participants in their own health care.

For more information as to how sex/gender-based biology and medicine have identified key differences in disease physiology between men and women, we invite readers to visit the Society of Women's Health Research web site (www.womenshealthresearch.org) and review "Just the Facts," as well as to read the groundbreaking 2001 Institute of Medicine report, *Exploring the Biological Contributions to Human Health: Does Sex Matter?*

Resources

WomensHealth.gov – The Federal Source for Women's Health Information

<http://www.4women.gov/>

Women's Health Centers for Disease Control and Prevention

<http://www.cdc.gov/women/>

Women's Health Medline Plus

<http://www.nlm.nih.gov/medlineplus/womenshealth.html>

Women's Health National Institutes of Health

<http://health.nih.gov/search.asp/28>

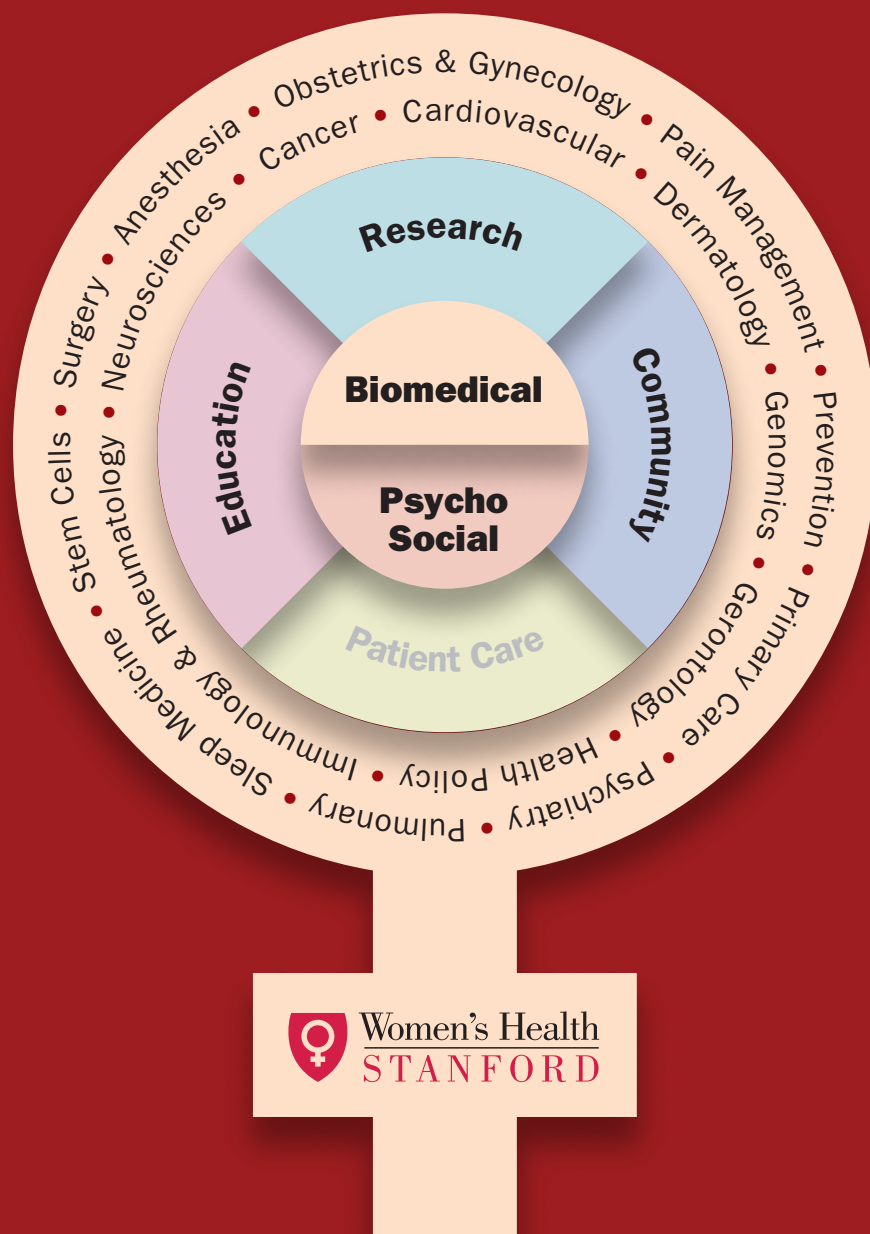
Society for Women's Health Research

<http://www.womenshealthresearch.org>

women's health program

mission statement

The Women's Health program, a multi-disciplinary program within the School of Medicine, based in the Department of Obstetrics and Gynecology, is dedicated to enhancing the health of women through the integration of biomedical and social science, by way of interdisciplinary, collaborative efforts, from a sex/gender-differentiated perspective. We are committed to expanding and fostering translational research by integrating basic, clinical and population science; as well as being a leader in women's health medical and community education programs.



mentoring scholars in women's health ... developing the medical leaders of tomorrow

Women's Health strives constantly to expand and improve on professional education in women's health. We seek to aid in the training of professionals who will do the necessary gender-based research towards providing the preventive care and therapies needed by women in our society. A new paradigm for understanding, preventing, and treating the health problems of women can be created by training physician-researchers across disciplines and across the life span.

Women's Health is taking an active role in facilitating the training of scientists who can pursue both basic and clinical research into disease processes in women. It is anticipated that these trainees will become independent investigators in basic, translational, and clinical research relevant to women's health, who will continue to focus their careers on expanding knowledge of health in women across the life span.

Jonathan Berek, MD, MMS, Professor and Director of the Department of Obstetrics & Gynecology, and Co-Director of the Women's Cancer Program at the Stanford Cancer Center, embodies and leads Stanford's integrated effort to develop leading medical scientists and clinicians, in Women's Health. "The future of Women's Health medical care is directly impacted by our ability to mentor young scholars. Stanford's ability to engage so many senior faculty – from an array of medical specialties – to volunteer to train young scholars, illustrates the priority and commitment we have to ensuring future gains in the quality of health care for all women," says Berek.

Dr. Berek personally directs two National Institutes of Health mentoring programs for junior Stanford faculty, the Women's Reproductive Health Research (WRHR) and Building Interdisciplinary Careers in Women's Health (BIRCWH) programs ... as well as providing oversight to other Women's Health training and mentoring programs for Fellows, Residents, medical students and Stanford undergraduates.

Building Interdisciplinary Research Careers in Womens Health (BIRCWH) Career Development Center

The theme of the Interdisciplinary Women's Health Research (IWHR) Career Development Program at Stanford University is advanced, rigorous mentoring in women's health research from bench to bedside. The program provides IWHR Scholars with structured, interdisciplinary research and didactic experiences, concomitantly with mentoring by experienced researchers and physician-scientists. It accommodates trainees with varying levels of experience in women's health research



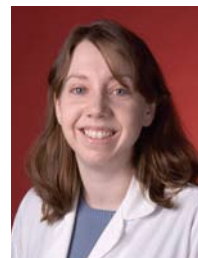
Dr. Jonathan Berek



Brendan Carvalho,
MBBCh, FRCA, MDCH



Christy Dosiou, MD, MS



Allison Kurian, MD, MSc



Nihar Nayak, PhD, DVM

and derives from a broad based initiative with research, mentoring, and trainee evaluation as cornerstones of the program. The goal of the IWHR Career Development Center is to bridge the time period between clinical or research training with independent research careers and to foster the development of future leaders in women’s health research in the United States.

BIRCWH Scholar	Research Project	Faculty Mentor(s)
Brendan Carvalho, MBBCh, FRCA, MDCH Assistant Professor of Anesthesia	Acute and Chronic Persistent Pain Following Cesarean Delivery: The role of cytokines	David Clark, MD, PhD Martin Angst, MD
Christy Dosiou, MD, MS Assistant Professor of Medicine – Endocrinology/Gerontology and Metabolism	Peripheral Blood Leukocyte Gene Expression in Women with Recurrent Pregnancy Loss	Marcia Stefanick, PhD
Allison Kurian, MD, MSc Assistant Professor of Medicine – Oncology	Risk Factors, Early Detection and Prevention of Breast and Ovarian Cancer	James Ford, MD Alice Whittemore, PhD
Nihar Nayak, PhD, DVM Assistant Professor of Obstetrics & Gynecology	Angiogenic factors and the role of progesterone in endometrial bleeding	Marlene Rabinovitch, MD Maurice Druzin, MD

Principle Investigator Program Director Administrative Director Administrative Associate
Jonathan Berek, MD, MMS Marcia Stefanick, PhD Jim Batterson Tracy Lindsay

Women’s Reproductive Health Research (WRHR) Career Development Center

The Women’s Reproductive Health Research (WRHR) Career Development Center at Stanford University, which is housed in the Department of Obstetrics and Gynecology, provides advanced basic and clinical research training and career development in women’s reproductive health research for obstetrician-gynecologists. The program accommodates trainees with varying levels of research experience and derives from a broad-based initiative with research, mentoring, and trainee evaluation as cornerstones of the program. The goal of the WRHR Career Development Center is to bridge the time period between clinical training with independent research careers and to foster the development of leaders in women’s reproductive health research.

WRHR Scholar	Research Project	Faculty Mentor(s)
Leah Millheiser, MD Instructor of Obstetrics & Gynecology	Peripheral Blood Flow in Pre- and Post-Menopausal Women	Bruce Arnow, PhD
Lisa Rahangdale, MD Instructor of Obstetrics & Gynecology	Endometrial characteristics of HIV-shedding and influence of microbicides on the upper genital tract	Dennis Israelski, MD Yvonne Maldonado, MD
Mylene Yao, MD Assistant Professor of Obstetrics & Gynecology	Microsystems-based High Throughput Experimental System for the Mammalian Oocyte	Stephan Quake, PhD

Principle Investigator Program Director Administrative Director Administrative Associate
Jonathan Berek, MD, MMS Maurice Druzin, MD Jim Batterson Tracy Lindsay



Mylene Yao, MD



Leah Millheiser, MD



Lisa Rahangdale, MD

mentoring scholars in women's health

continued from page 5

Stanford Undergrads Gain Medical Research Experience in Women's Health

The Women's Health program has been active to pairing Stanford undergraduate students with medical faculty, for the purpose of enhancing each student's research knowledge and experience.

Past scholars have spent extensive time in research being conducted in a variety of women's health medical disciplines, from gynecologic oncology to cardiovascular disease to reproductive biology. Students have had opportunities in basic, translational, clinical and population research.

This program, led by principal investigator Lynn Westphal, MD and Marcia Stefanick, PhD, is currently recruiting five Stanford undergraduate scholars for summer 2008 placement. Research mentors and projects will come from different specialties, but will cover women's health interdisciplinary work in cancer; cardiovascular medicine; immunity; neuroscience; and stem cells or reproductive biology. Selected scholars will receive an orientation to our core basic science lab, directed by Nihar Nayak, PhD, DVM and be required to write a paper about their experience, that will be presented at a special edition of our Littlefield Women's Health Medical Forum.

Dr. Westphal has been a particularly enthusiastic advocate for beginning our mentoring activity at the undergraduate level. In addition to this program, she has supported undergraduate efforts at producing a women's international health symposium (February 2008 – thinkBIG) and regularly makes time for advising students on career growth in women's health medicine.

Dr. Stefanick brings her expertise and commitment to undergraduate education to the classroom, where she has regularly held courses for Stanford undergraduates, particularly Human Biology majors. Her newest course, *Sex Differences in Human Physiology and Disease*, debuted winter quarter 2008.



Marcia Stefanick, PhD



Lynn Westphal, MD



Mary Jacobson, MD

Scholarly concentrations ... Mentoring Medical Students in Women's Health

The Stanford University School of Medicine (SoM) has long been a leader in educating its medical students. The Scholarly Concentration (SC) program, introduced in 2004, is a shining example of Stanford's innovativeness in medical education. Women's Health has been a key component of the SC program since its inception.

The SC program provides medical students with faculty-mentored scholarly experiences in the areas of individual interest combined with structured coursework to support this scholarship. This required component of the MD curriculum develops critical thinking, skills in evaluating new data, and hands-on experience with the methods by which new scholarly information is generated.

The program offers 12 areas of study, including seven Foundation areas, and five Application areas. The Foundation areas are designed to develop skills and tools that can be applied to important areas of health care (e.g. clinical research). The Application areas - Women's Health; Cancer Biology; Cardiovascular Pulmonary; Immunology; and Neuroscience - represent the prominent, large interdisciplinary programs found in the SoM.

The Women's Health program for medical students, led by Co-Directors Lynn Westphal, MD; Marcia Stefanick, PhD; Mary Jacobson, MD and Jim Batterson and Tracy Lindsay, provides medical students an opportunity, via a core curriculum, mentored research and exposure to related medical seminars, to enhance their multidisciplinary understanding of Women's Health.

The Women's Health Application program graduated its first scholar in June 2007 (Laura Edgerley, MD) and currently mentors 13 other current medical students.

Courses that make up our core curriculum: Sex Differences in Human Physiology and Disease; Controversies and Topics in Women's Health; Women's Health Medical Forum; and Women's Health Independent Project. Additionally, students must engage in a separate, medical scholars research project.

In addition to their director roles in this Stanford program, Drs. Westphal and Jacobson are preparing to contribute their knowledge of this innovative SC program to colleagues nationally, as Stanford faculty share this expertise to elevate the medical education of students everywhere.

Women's Health Scholarly Concentration Application Area

2007 - 2008 Scholars

Bory Kea	Yingbing Wang	Adeoti Oshinowo	Sha-Nita Jones
Hanna Kim	Jenny Wilson	Kate Pettit	Cara Liebert
Bryan Maxwell	Tress Goodwin	Josephine Czechowicz	
	Jessica Les	Carolyn Fredericks	

Directors

Lynn Westphal, MD; Mary Jacobson, MD; Marcia Stefanick, PhD

Administrative Director

Jim Batterson, Executive Director, Women's Health

Administrative Associate

Tracy Lindsay

pediatric & adolescent gynecology

new specialty program caters to the unique health issues of girls



Paula Hillard, MD



Judy Lacy, MD

Program Description

The Stanford Program for Pediatric and Adolescent Gynecology was established to provide expert medical care in a caring and sensitive environment designed to be particularly responsive to the unique needs of adolescents and children with gynecologic needs.

Drs. Paula Hillard and Judy Lacy see patients for evaluation and consultation. They will work actively with referring clinicians to facilitate diagnosis, treatment and management. They are available to speak by phone with clinicians who have questions about management or referral through the LPCH Physician Referral Center at 888-ASK-LPCH (888-275-5724) or the Stanford Referring Physician Resource Center at (866) 742-4811

About the Program Directors

Led by renowned clinician and researcher, Paula Hillard, MD, the Pediatric & Adolescent Gynecology program at Stanford is among the very few such programs in the country.

Dr. Hillard, Professor of Obstetrics & Gynecology and Division Director for Gynecologic Specialties, is a leading authority on Pediatric & Adolescent Gynecology, serves on several government and medical profession boards, is a popular speaker and a frequent source for medical media reporters.

Judy Lacy, MD, received her medical degree from the Oregon Health and Sciences University, completed her internship and residency at Duke University Medical Center, and her fellowship in Pediatric & Adolescent Gynecology at the Hospital for Sick Children, University of Toronto.

Drs. Hillard and Lacy welcome girls of all ages for compassionate, expert medical care at both the Stanford Gynecology clinic location as well as at the Castro Commons satellite site of the Lucille Packard Children's Hospital.



The Program for Pediatric and Adolescent Gynecology offers a comprehensive range of services for the evaluation, diagnosis and treatment of adolescents and children with gynecologic disorders including, but not limited to:

Preventive health and guidance for teens and parents

Menstrual problems

- Heavy bleeding
- Frequent bleeding
- Infrequent bleeding (Oligomenorrhea)
- Absent menstrual periods (amenorrhea)
- Menstrual suppression in girls with developmental delay or complex medical problems.

Genital (vulvar or vaginal) infection or pain

- Vulvovaginitis
- Itching and irritation
- Lichen sclerosis

Abnormal Pap smear

Ovarian cysts and masses

- Pain

Pelvic pain

- Menstrual pain (dysmenorrhea)
- Endometriosis
- Chronic pelvic pain

Gonadal Dysgenesis

- Turner syndrome

Endocrine (Hormonal) problems

- Polycystic Ovarian Syndrome (PCOS)
- Early or delayed puberty
- Precocious or early puberty

Pregnancy-related problems in Adolescents

- Unintended pregnancy

Pregnancy prevention (contraception)

- Implanon
- IUDs
- Other contraceptive options and medical risks

Breast problems

Adolescent Sexual Health

Congenital Anomalies

- Vaginal septum
- Imperforate hymen
- Absent uterus and vagina

Clinical Appointments

650-725-6079

Gynecologic Specialties Clinic

Blake Wilbur Building
900 Blake Wilbur Drive
2nd Floor, W2080
Stanford, CA 94305

Lucile Packard – Castro Commons Clinic

Adolescent Medicine
1174 Castro Street, Suite 250
Mountain View, CA 94040
(650) 694-0600

Physician Referrals

800-756-5000

referral@stanfordmed.org

888-ASK-LPCH (888-275-5724)

referral@lpch.org

Clinical Research Studies

<http://womenshealth.stanford.edu/research/trials/gyn>

Links

Gynecologic Specialties
<http://obgyn.stanford.edu/gyn>

North American Society for
Pediatric and Adolescent
Gynecology
<http://www.naspag.org>

women's heart health at stanford



integrating research, education and clinical care
to enhance cardiovascular health for women

In 2006, Stanford Cardiovascular Institute director Robert C. Robbins, MD announced a new program for women's cardiovascular health at Stanford.

The Mission of "Women's Heart Health at Stanford"

- Enhance cardiovascular clinical care for women
- Provide women's cardiovascular education in the surrounding communities and the Stanford academic community
- Advocate and establish new research on sex differences in heart and vessel disease at Stanford and nationally

interviewed and sought-after as a speaker nationally and internationally.

Clinical Director

Jennifer Tremmel, MD, SM (Epidemiology).

Dr. Tremmel is an Instructor and Interventional Cardiologist in the Division of Cardiovascular Medicine. She also trained in Preventive Cardiology and was a Postdoctoral Research Scholar at the Stanford Prevention Research Center. Dr. Tremmel is the Clinical Director of Women's Heart Health at Stanford, as well as the Director of the Stanford Secondary Prevention Program. Dr. Tremmel's research interests include sex differences in coronary artery disease, the determinants of vascular access complications, and the effects of weight on coronary physiology and cardiac outcomes. She has also evaluated the use of drug-eluting stents in transplant arteriopathy and keeps Stanford's Tako-Tsubo Patient Registry. She is currently investigating sex differences in the occurrence of coronary endothelial dysfunction, diffuse plaque deposition, and microvascular disease in women and men presenting with chest pain, but having "normal" coronary arteries by angiography.

Nurse Practitioner,

Mary P. Nejedly, RN, MS, NP-C

Mary is the primary contact for the women's heart health clinic and provides evaluation for cardiac risk assessment and management of primary and secondary prevention. She is a specialist in lipid evaluation and treatment and stresses the importance of lifestyle modification in conjunction with pharmacologic interventions. She received her Masters of Science degree as an Adult Nurse Practitioner from the University of California at San Francisco. She has over 25 years of nursing experience including the coronary care unit (CCU), heart failure, lipid management, general cardiology, and primary care.

Leadership

Co-Director

Hannah Valentine, MD, Professor of Cardiovascular Medicine

Dr. Valentine, a cardiologist, is Senior Associate Dean for Diversity and Leadership at Stanford University Medical Center. She is President of the Western States Affiliate Board of the American Heart Association and a frequent speaker at national and international meetings on heart disease and women's issues.

Co-Director

Marcia Stefanick, PhD, Professor of Medicine-Prevention Research, and, by courtesy, of Obstetrics and Gynecology

Dr. Stefanick is active in a national Think Tank of cardiologists and researchers focused on Women and Heart Disease, is promoting the Investigation of Sex and Gender Differences in Cardiovascular Research across the wide spectrum of research areas represented by Stanford CVI members, and is an acknowledged expert on women's health issues (especially cardiovascular) and disease prevention, is frequently



Hannah Valentine, MD



Marcia Stefanick, PhD

Women's Heart Health at Stanford Clinical Director

Jennifer Tremmel, MD and her associate, Mary Nejedly, NP, utilize the following internal network of Stanford colleagues to ensure optimal, comprehensive care for all patients:

Hannah Valantine, MD (Heart Failure/Transplant)
Ingela Schnittger, MD (Valvular Heart Disease)
Paul Zei, MD (Electrophysiology)
Tracey McLaughlin, MD (Endocrinology)
Michael McConnell, MD, MSEE (Cardiovascular Imaging)
Jane Borchers, MPH, RD (Nutrition)
Mytilee Vermuri, MD (Psychiatry)
Robert Robbins, MD (Cardiothoracic Surgery)
Wei Zhou, MD (Vascular Surgery)
Mary Jacobson, MD (Gynecology)

Women's Heart Health at Stanford Committee

Marcia Stefanick, PhD
Medicine – Stanford Prevention Research Center

Hannah Valantine, MD
Cardiovascular Medicine

Jennifer Tremmel, MD, SM
Cardiovascular Medicine

Jim Batterson
Executive Director, Women's Health

Kathy Berra, MSN, ANP, FAAN
Stanford Prevention Research Center

John Cooke, MD, PhD
Cardiovascular Medicine

Sharon Hunt, MD
Cardiovascular Medicine

Nishita Kothary, MD
Diagnostic Radiology

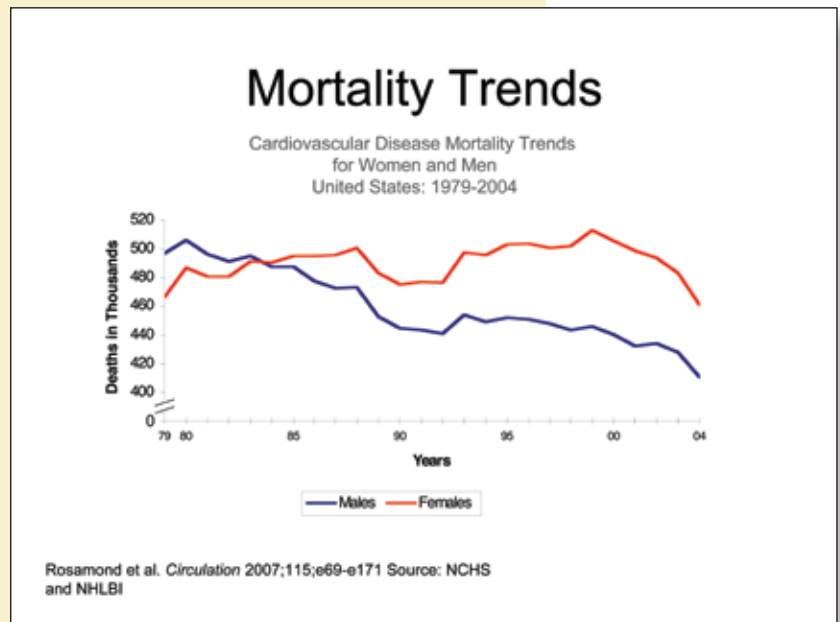
Mike McConnell, MD, MSEE
Cardiovascular Medicine

Marlene Rabinovitch, MD
Pediatric Cardiology

Natalie Rasgon, MD, PhD
Psychiatry

Ingela Schnittger, MD
Cardiovascular Medicine

Mary Sweeney, MD
Cardiovascular Institute Program Manager



women's hearts take center stage at new stanford clinic

By Tracie White

Months after joining an exercise group, Valerie Garcia would stay red in the face, gasping for air, feeling like she was going to pass out, while the rest of her classmates jogged by. No matter how hard or how often she exercised, she was incapable of building any endurance.

"I was sure it wasn't my heart but nothing else was helping," said Garcia, who is 48. Her asthma doctor gave up on a diagnosis and referred her to the new women's cardiovascular clinic, Women's Heart Health at Stanford Hospital & Clinics.

She underwent stress testing and was found to have a possible narrowing in a heart artery, so she had an angiogram. That showed nothing. But after additional specialized testing, which examines the function of the heart vessels, Garcia was diagnosed with "marked endothelial dysfunction," a form of heart disease that often goes undetected and undiagnosed in women.

It utterly caught Garcia off guard. She had never even considered that she might have heart disease.

"I could have easily been dismissed, but they're specifically interested in women," said Garcia about her treatment at the women's clinic. "You can feel it."

Diagnosing and treating women who might

otherwise slide under the radar screen is the goal of Stanford's quickly growing women's heart clinic, which opened less than a year ago, said clinic director Jennifer Tremmel, MD, who is also an instructor of cardiovascular medicine at the Stanford University School of Medicine. The specialized clinic operates one day a week at Stanford Hospital and twice a month at a clinic in Monterey, and has about 150 patients.

As part of a growing trend across the nation to set up cardiology programs for women, the new clinic is designed to reach out to those who for a variety of reasons—less aggressive care, differing risk factors, gaps in research—are getting missed. The clinic is also part of the Stanford Cardiovascular Institute's overarching goal to address issues of women's heart health through patient care, education and research in the areas where huge gaps in knowledge remain.

"We can find out what's wrong with these patients," Tremmel said. In addition to treating women, she is conducting an American Heart Association-funded study on sex differences in cardiovascular disease. "We can diagnose them, we can treat them. Most physicians are going to stop early. We keep going."

While women are generally more likely to worry about breast cancer, the reality is that cardiovascular disease kills almost twice as many American women as all cancers put together. It's the largest single cause of mortality among women, accounting for 38 percent of all deaths among females, according to the American Heart Association.

And yet, consistently, heart disease in women is misdiagnosed and under-treated.

Most disturbing, women have not had the decrease in death rates from heart disease that men have continued to experience over the past few decades. More women than men have died of cardiovascular disease in every year since 1984. Exactly why this is happening remains unclear.

WOMEN'S
HEART HEALTH
at STANFORD

Jennifer Tremmel, MD,
Clinical Director, Women's
Heart Health at Stanford.



“The sex gap in cardiovascular disease hit its peak in 1999 and is finally getting some attention,” Tremmel said.

This is where a clinic specifically targeting women can step in and help, Tremmel said. As an expert on women’s heart health, she keeps up to date on research, and after treating so many women, she’s more attuned to their different needs. “It’s amazing how similar all these women are when you get them together in one clinic,” she said.

For example, while women and men suffer many of the same symptoms of heart disease, such as chest pain or shortness of breath, women tend to complain of additional symptoms. They may experience back, neck or arm pain as well, and they often report getting their symptoms when under emotional stress. “When women come in and list off several symptoms, it’s confusing to know what’s wrong with them,” Tremmel said. “In the past we called them atypical, but I see so many women with these symptoms, they’re now typical to me.”

Women historically haven’t been included in scientific studies to the extent that men have. But there has been a push within the past decade to conduct more research on women’s cardiovascular disease, such as the National Institutes of Health-sponsored study called the Women’s Ischemia Syndrome Evaluation. That study found that just because a woman’s arteries appear clear on routine tests like an angiogram, it doesn’t mean she has normal coronary arteries.

Additional testing that evaluates for microvascular disease, diffuse non-obstructive plaque or endothelial dysfunction may be revealing.

“The WISE study has been pivotal in shaping my research career,” Tremmel said. “Up to 20 percent of patients with symptoms are found to have normal-appearing arteries in the cath lab. We tell them that they are fine, but they continue to have symptoms and we have no good explanation. It’s extremely frustrating for doctors and patients.”

Tremmel is conducting a study that will expand on the WISE results, comparing rates of microvascular disease and endothelial dysfunction in men and women.

But for now, she’s finding that additional vascular function testing, such as the endothelial dysfunction test that uncovered Garcia’s disorder, can successfully pinpoint heart disease problems in previously undiagnosed female patients.

“We’re finding it just doesn’t work to treat women like men using data derived from men,” Tremmel said. “There’s enough data out there that we can start treating women like women and hopefully it will lead to an improvement in outcomes and a reduction in the gender gap.”

Garcia’s endothelial dysfunction test involved administering a medication into her coronary artery at the time of her catheterization, which is a technique used to insert a catheter into the arteries. The test found that the lining of the artery was actually causing the artery to constrict during times of exercise when it should be dilating.

Garcia is 48, younger than the average female heart patient, who is usually in her 60s or older. She’s thin, exercises regularly and has low blood pressure. But a smoking habit that she quit 18 years ago could have been the cause of her problems, which, if left untreated, could lead to a serious heart condition.

“She didn’t have a lot of risk factors,” Tremmel said. “The routine test didn’t show anything. She had normal-appearing arteries. What we did that’s different from the routine was the vascular function tests.”

Since her diagnosis and treatment with oral medication, a long-acting nitrate, Garcia has increased her jogging distance from a half-mile to 2 miles without feeling like she’s going to faint. “They were grilling me, ‘Do you have chest pain? Do you get light-headed?’” She added, “They really listened to me.”

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MAKE AN APPOINTMENT

Stanford Office

Cardiology Clinic
Boswell Building
300 Pasteur Drive
Stanford, CA 94305

New Patients
(650) 736-0516

Return Appointments
(650) 723-6459

Fax
(650) 724-1444

E-mail
herheart@stanford.edu

Appointment Hours
Tuesday, 8:30 am – 4:30 pm
M-F, 9 am – 4 pm as needed

Monterey Office

880 Cass Street, Suite 108
Monterey, CA 93940

New Patients
(831) 649-9330

Return Appointments
(831) 649-9330

Fax
(831) 649-9335

E-mail
herheart@stanford.edu

Appointment Hours
Fridays, 11 am – 4:30 pm

International Patients

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IMS@stanfordmed.org

what are women cardiovascular patients asking?

Women's Health Magazine asked Jennifer Tremmel, MD, Director of Women's Heart Health at Stanford clinical program, to answer a series of questions, frequently asked by her female cardiovascular clinic patients.

I've always had the feeling that cardiovascular disease is more of a man's disease. Why is there now such an emphasis on women?

Cardiovascular disease has been the leading cause of death in women for decades, but only recently is it getting the attention it deserves. In fact, since 1984, more women than men have died from cardiovascular disease every year. There are several important reasons that we have learned to associate cardiovascular disease with men and these should not be overlooked. First, cardiovascular disease is also the leading cause of death in men. Second, cardiovascular disease is actually more common in men than women. Third, because of the higher rates of disease in men, most of the research in cardiovascular disease has been done on men. Consequently, death rates from CVD have been steadily declining for men over the past two decades, while rates have been relatively stable in women. This has resulted in a growing sex gap (see graph) and has prompted more scientific research studies about women and cardiovascular disease, as well as campaigns to raise awareness of heart disease in women. In turn, there has been an increase in public information and education about women and heart disease and this is why you now so commonly hear about it.

How can I determine if I'm at risk? How is my risk different from a man's risk?

It is important that you know your risk of heart disease. The risk factors for heart disease are the same in women and men, but their relative importance varies between the sexes. For example, diabetes and impaired fasting glucose (an elevated blood sugar level) have been shown to confer an even greater risk in women than in men. Likewise, smoking

is felt to be worse for women than men. While an elevated triglyceride level and low HDL (good cholesterol) are independent predictors of heart disease in both women and men, they appear to have greater predictive potential in women. On the other hand, an elevated LDL (bad cholesterol) is more predictive of coronary risk in men. Finally, both obesity and a sedentary lifestyle are risk factors for heart disease, but more women than men carry excess weight and do not engage in physical activity. In addition to the traditional risk factors, it may be helpful to know if you have other markers of risk, such as an elevated C-reactive protein (CRP) or lipoprotein (a). Also, mental stress and depression are more common in women and can have an adverse effect on your heart. You can assess your risk online at www.womensheart.stanfordhospital.com.

At what age should I start worrying about my risk of heart disease?

Women (and girls) of all ages should be concerned about their risk of heart disease. Healthy habits start early and neglecting risks leads to an accumulation of your total risk over time. Staying physically active and maintaining a healthy weight should be goals for everyone. Childhood obesity and diabetes are on the rise and may soon have a significant impact on heart disease rates in young people. Having your blood pressure periodically checked is important, even for children and adolescents. It is recommended that everyone have their cholesterol checked at the age of 20 and at least every 5 years after that. If there is someone in your immediate family (parent, sibling, or child) with premature heart disease (a male relative <55 or a female relative <65) then you need to be particularly concerned about your risk and may want to have your cholesterol checked sooner. While we consider post-menopausal women to be at an increased risk of heart disease, your risk increases steadily over time from an early age. You may be surprised to learn that heart





disease is the third-leading cause of death for women age 25 to 44 years and the second-leading cause of death for women 45 to 64 years.

What symptoms should I be concerned about? How do these symptoms differ from men's?

The most common symptom of coronary artery disease in both women and men is chest pain during exertion. Remember, though, that while doctors use the term chest “pain”, it doesn't always feel like pain. It may actually feel like a pressure, tightness, or squeezing. There is often accompanying shortness of breath, and the discomfort may radiate down the arms or into the jaw. While women will generally have symptoms similar to men, they often report more symptoms, including abdominal pain, neck pain, or fatigue. Women are also more likely than men to get their symptoms with rest or during emotional stress, or during their menstrual period if they are pre-menopausal. Women's symptoms are often considered “atypical”, but I hear so many women with these “atypical” symptoms that they have become very typical to me. Because women are less aware of the symptoms they should be concerned about, or because they think that heart disease couldn't happen to them, they often present for medical care later than men. This may explain, in part, why women have worse outcomes than men.

What should I do if I'm having symptoms but I don't know if they're from my heart?

It is always better to be safe than sorry. If you are periodically having symptoms that you think are coming from your heart, you should consult with your physician. He or she may order a stress test just to be sure. He or she may also consider other possibilities such as asthma, acid reflux, or a pulled muscle. These diagnoses should only be considered after heart disease has been ruled out. Unfortunately, women are less likely to receive testing for heart disease, perhaps because they are considered to be lower risk

or because their symptoms sound “atypical”, and this is another possible explanation for why women have worse outcomes than men. If your doctor hears about your symptoms, but doesn't bring up the possibility of heart disease, it never hurts to specifically ask him or her if heart disease is a possibility. I always encourage women (and men) to be pro-active in their healthcare. If you are having severe symptoms that aren't going away, you may be having a heart attack and should call for emergency medical help immediately.

I have been told that my arteries are normal, but I still have chest discomfort and shortness of breath. What should I do?

Some women continue to have their symptoms even though it appears that heart disease (and often many other diagnoses) have been ruled out. While our current testing (stress testing and angiography) is good for ruling out narrowings or blockages in the coronary arteries, it does not always rule out functional problems of the coronary arteries. These functional problems include endothelial dysfunction and microvascular disease. Endothelial dysfunction occurs when the cells lining the coronary arteries become damaged and start to constrict when they should dilate. Microvascular disease is when the small vessels that we can't see on angiography become dysfunctional or plugged and don't easily allow blood to the heart muscle. This is an area in which I am currently doing research. It has been found that women with symptoms of heart disease, but normal-appearing coronary arteries, often have endothelial dysfunction, microvascular disease, or diffuse non-obstructive plaque. What we don't know is if these findings are actually more common in women than men. I am testing both women and men to determine if there is a difference in vascular functional abnormalities between the sexes. The testing is specialized and requires an invasive procedure so it is only performed

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cardiovascular

what are women cardiovascular patients asking?

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on patients who are felt to need a cardiac catheterization (angiogram). In patients who don't want/need invasive testing, we often try empiric treatment to see if it helps. In addition to medications that can help with the symptoms, lifestyle modification (diet, exercise, and weight loss) are key components in the treatment plan.

How is going to a women's cardiovascular health clinic different from going to a general cardiology clinic?

Women have traditionally been treated based on research that has been done on men. While men have had an improvement in their outcomes over the decades, women have not fared as well. We have a growing body of research showing that there are sex difference throughout cardiovascular disease, from risk factors to symptoms and from testing to treatment and outcomes. Unfortunately, many physicians continue to care for women and men similarly, and many physicians continue to treat women less aggressively. It has been shown that women get less diagnostic testing than men, are not always prescribed proven medications, and are often not achieving the minimum recommendations of prevention guidelines. In our women's cardiovascular health clinic we aim to treat a woman like a woman, using the most up-to-date, evidence-based data on women's cardiovascular disease. We take this information into consideration when defining your risks, listening to your symptoms, ordering your tests, and treating your problems. We also try to take in the whole patient, recognizing that social and psychological factors can play a large role in your symptoms and cardiovascular health. Our hope is that caring for women in this way will ultimately lead to an improvement in their outcomes.

I am getting close to menopause. What changes should I watch for that might increase my risk of heart disease?

As women go through menopause, many changes take place. Women tend to put on weight and have a decrease in their exercise tolerance. In addition, their cholesterol profile often changes. HDL (good cholesterol) tends to go down, while triglycerides and LDL (bad cholesterol) tend to go up. Along with that, the LDL phenotype often changes so that women develop more small, dense LDL (more atherogenic), replacing their large, buoyant LDL (less atherogenic). Women also experience many symptoms during menopause that can be confusing to both them and their health care provider. They often feel more fatigue, don't sleep as well, have hot sweats, may notice more palpitations, or even chest pain. They may also notice more emotional problems such as anxiety, depression, or irritability. Menopause is as important a time as any to persist with healthy lifestyle behaviors such as maintaining weight and getting regular physical activity.

I have heard that hormone therapy is bad for your heart, but I'm having terrible hot flashes and can't sleep. What do you recommend?

It was originally thought that hormone therapy would be good for women's hearts because estrogen has many beneficial effects on the cardiovascular system and also positively affects certain cardiac risk factors, such as cholesterol. However, studies have shown that hormone therapy does not protect the heart and may be harmful. Women over the age of 70 or greater than 20 years from menopause, in particular, have increased rates of cardiac events (within the first year of taking hormone therapy). There does not appear to be quite the same risk in younger women, but they also have an increased risk of stroke, blood clots, and breast cancer. I think the decision to start hormone therapy is best done in conjunction with both your cardiolo-





gist and gynecologist, who can together help you weigh the risks and benefits. The current recommendation is that women only take hormone therapy for moderate to severe vasomotor symptoms (hot flashes, night sweats, etc), and that when doing so, they take the smallest effective dose for the shortest possible time.

I don't have an existing heart condition or any symptoms of heart disease. How can Women's Heart Health at Stanford benefit me?

Women's Heart Health at Stanford provides a cardiac risk assessment for women without existing heart conditions or symptoms of heart disease. A risk assessment alerts you to your risk factors and helps you manage those risks to prevent heart disease. Your one-hour risk assessment visit is conducted by our nurse practitioner, Mary Nejedly, and includes a full history and physical exam, as well as blood cholesterol and glucose testing. Mary and I work as a team, so if she finds something that is concerning, she will consult with me or may even have you come in to see me for a full evaluation. Additional diagnostic testing may also be ordered if indicated, or we may recommend that you see one of the doctors in our Internal Referral Network. All of these doctors are committed to providing the same evidence-based, sex-specific care that we are. Finally, we will make our recommendations, which you may pursue on your own or with your regular doctor, or if you wish, you may continue to see Mary for ongoing risk factor modification counseling. In addition, once you are a patient in our clinic, I will always be available to you should you need to see a cardiologist. At the end of the visit, you will be given access to a computerized, personalized cardiac risk assessment with customized recommendations that you can update as your risk profile changes.

I have an existing heart condition or symptoms of heart disease. How can Women's Heart Health at Stanford benefit me?

Women's Heart Health at Stanford provides cardiology consultations and ongoing care for women with existing heart conditions or symptoms of heart disease. Your cardiology consultation may provide a diagnosis of your condition and/or recommend a course of treatment. When you first call in, we will decide if you should see me or if you have a special need that would be better served by one of the physicians in our Internal Referral Network. I see women who either have known coronary artery disease or there is a suspicion that they have coronary artery disease. We will meet for a one-hour visit and do a complete history and physical exam in order to determine what kind of care you need. Additional diagnostic testing may be ordered if indicated. A copy of your consultation will be sent to your primary healthcare provider, unless you indicate otherwise. Women with an established local cardiologist are accepted on a case-by-case basis for a second opinion. Once you are established in our clinic, Mary and I will work together to treat your symptoms and optimize your risk factors.

The mission of our clinic is to improve the cardiovascular health of women by offering evidence-based, sex-specific, personalized, and comprehensive care including primary and secondary prevention, diagnosis, and treatment of cardiovascular disease. It is our hope that caring for women in this way will help them to live longer, healthier lives.

cardiovascular
faq's

female sexual medicine

Program Description

Female sexual dysfunction (FSD) affects 43% of women, yet it continues to be one of the most underdiagnosed medical problems in the United States today. It is classified by four disorders, including: hypoactive sexual desire disorder, sexual arousal disorder, orgasmic disorder, and pain disorders (vaginismus and dyspareunia). The evaluation and treatment of FSD is a multi-disciplinary process, integrating physiologic and psychological approaches. FSD not only affects a woman's quality of life, body image, and relationship, but may also serve as a marker of a serious underlying medical disease such as diabetes, peripheral vascular disease, or depression.

The Female Sexual Medicine Program, within the Division of Gynecologic Specialties at Stanford University Medical Center, specializes in the evaluation and care of sexual dysfunction. Patients benefit from novel treatments as well as the opportunity to participate in cutting-edge research studies. The program incorporates certified sex therapists, pelvic floor physical therapists, and mental health clinicians when creating comprehensive treatment plans for each patient.

A sexual complaint should never be ignored. The most challenging aspect of treatment is taking the first step to acknowledge the problem and seek

help. The Female Sexual Medicine Program aims to take the anxiety out of this process through the efforts of a highly-experienced team.

About the Program Director

Leah Millheiser, MD, faculty physician and researcher in the Division of Gynecologic Specialties, Department of Obstetrics & Gynecology, is the founder and Director of the Female Sexual Medicine Program.

One of the country's leading authorities on female sexual health, Dr. Millheiser is a sought after speaker at medical conferences, patient education events and a frequent guest on television and radio programs. Dr. Millheiser has been recognized by the National Institutes of Health by way of being named a Women's Reproductive Health Research Scholar, a special honor enjoyed by few American physician researchers.

She received her undergraduate degree from Columbia University, New York City; graduated from Northwestern University School of Medicine, Chicago; and did her residency in obstetrics & gynecology at Stanford University.

Dr. Millheiser looks forward to helping all women seeking confidential, compassionate, personalized assistance with any issues impacting their sexual health.



Leah Millheiser, MD

ask dr. millheiser questions about female sexual function

Q I have been using a water-based lubricant during sex with my husband for the past two years. Since that time, I have noticed that I am getting frequent yeast infections. Could this be due to the lubricant or is this just a result of getting older and a change in hormones? I thought that water-based lubricants were the safest to use.

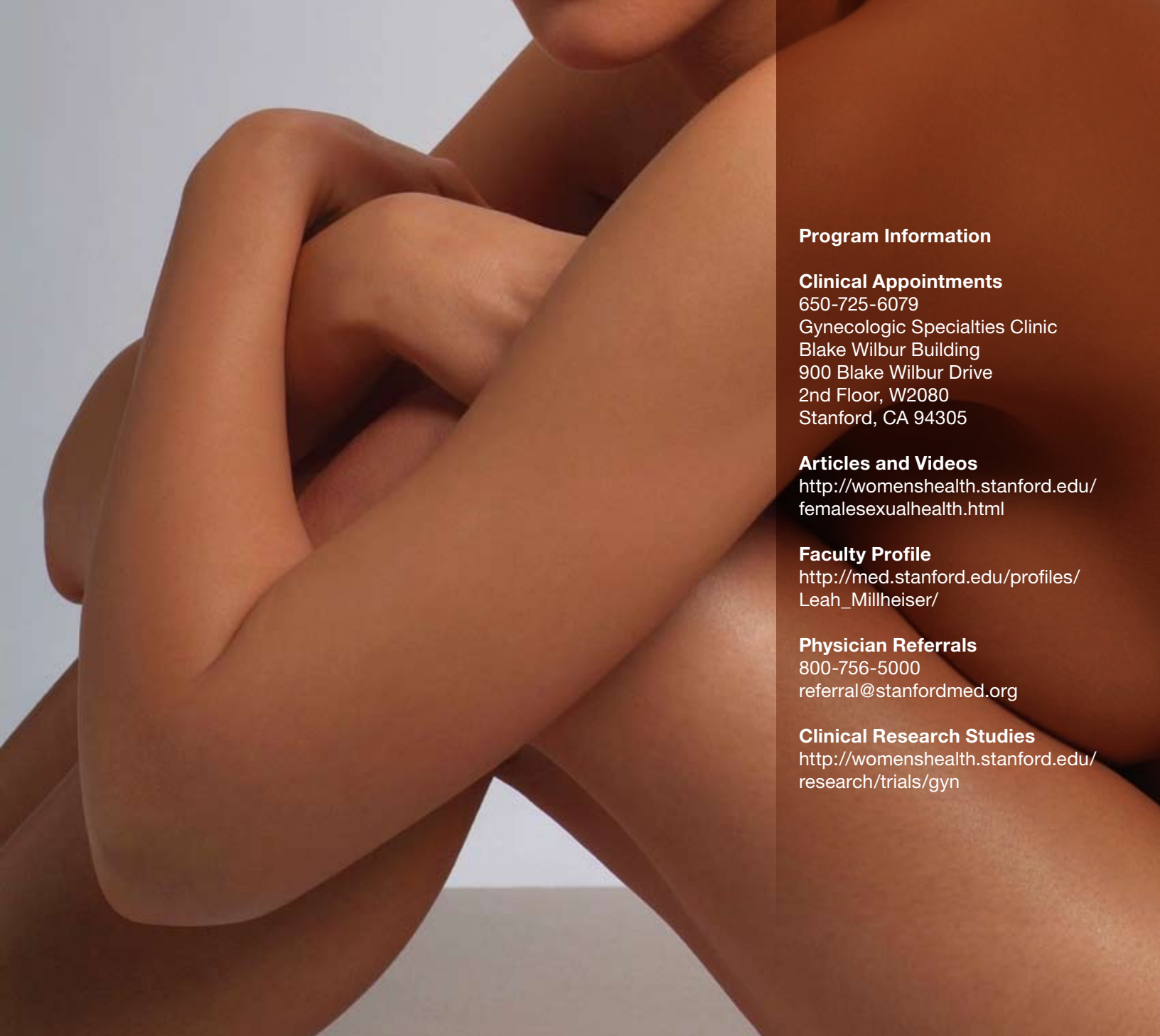
Dr. Millheiser: You are absolutely right! Water- and silicone-based lubricants are the safest to use for two reasons: they don't break down latex condoms (this can occur with mineral- or petroleum-based lubricants) and they will not promote vaginal inflammation. However, many of these water and silicone lubricants have glycerin as an active component. Glycerin can cause yeast infections. Therefore, if you are prone to developing yeast infections, switch to the glycerin-free version of your favorite lubricant. Most companies today make them. If you can't find them in

your local pharmacy, you can usually buy them on-line.

Q My daughter is a teenager and wants to get the HPV vaccine. I am afraid that this will make her more likely to have sex, especially unprotected sex. Do you think it's a good idea?

Dr. Millheiser: The human papilloma virus (HPV) vaccine protects girls from the 4 most common types of the virus that cause genital warts and cervical cancer. However, there are other less common types that are not prevented by the vaccine. Safe sex practices are essential with or without the HPV vaccine and this is where early sexual education by a parent or caregiver is imperative. Studies show that when children learn about sexuality at home, they are less likely to engage in risky sexual behavior.

Q I am a woman in my twenties who has been married for about 8 months and I still have not had sex with



Program Information

Clinical Appointments

650-725-6079
Gynecologic Specialties Clinic
Blake Wilbur Building
900 Blake Wilbur Drive
2nd Floor, W2080
Stanford, CA 94305

Articles and Videos

<http://womenshealth.stanford.edu/femalesexualhealth.html>

Faculty Profile

http://med.stanford.edu/profiles/Leah_Millheiser/

Physician Referrals

800-756-5000
referral@stanfordmed.org

Clinical Research Studies

<http://womenshealth.stanford.edu/research/trials/gyn>

my husband. In my culture, sex is not appropriate before marriage. I love my husband and we have a great relationship. Every time we have tried to have sex, he feels like he is “hitting a brick wall”. I tell my body to relax, but my vagina doesn’t seem to be listening. What’s wrong with me?

Dr. Millheiser: Although it is impossible to diagnose you without doing an examination, it sounds like you may be suffering from vaginismus, one of the sexual pain disorders. This is a very common condition seen in young women. The muscles of the lower third of the vagina will contract involuntarily. So you are correct when you say that “your vagina isn’t listening to your brain”. Vaginismus can occur for many reasons: the fear of vaginal penetration and pain, the fear of pregnancy, the inability to give up control of one’s body, relationship difficulties, or a prior negative experience associated with sex. Sometimes, it occurs for no specific

reason at all. The great news about vaginismus is that it is easy to treat with vaginal dilator therapy and education.

Q I have been hearing a lot about Viagra for women. Is it safe for me to take my husband’s?

Dr. Millheiser: No!! It is not safe for a woman to use Viagra unless it is under the guidance of a physician. Viagra can be dangerous, even deadly, if used by a person with undiagnosed heart disease or who is taking certain medications, such as nitrates. Viagra should never be used recreationally. It has been shown to be effective only in women with vaginal arousal disorder or orgasmic disorder. However, if a woman is also experiencing low sexual desire or depression, Viagra may not be effective.

who is winning at losing (weight)?

stanford diet study – of more than 300 women –
tips scale in favor of atkins plan

The case for low-carbohydrate diets is gaining weight. Researchers at the Stanford University School of Medicine have completed the largest and longest-ever comparison of four popular diets, and the lowest-carbohydrate Atkins diet came out on top.

Of the more than 300 women in the study, those randomly assigned to follow the Atkins diet for a year not only lost more weight than the other participants, but also experienced the most benefits in terms of cholesterol and blood pressure.

“Many health professionals, including us, have either dismissed the value of very-low-carbohydrate diets for weight loss or been very skeptical of them,” said lead researcher Christopher Gardner, PhD, associate professor of medicine at the Stanford Prevention Research Center. “But it seems to be a viable alternative for dieters.”

The results are published in the March 7, 2007 issue of the *Journal of the American Medical Association*.

The 311 pre-menopausal, non-diabetic, overweight women in the study were randomly assigned to follow either the Atkins, Zone, LEARN or Ornish diet. Researchers chose the four diets to represent the full spectrum of low-to high-carbohydrate diets.

The Atkins diet, popularized by the 2001 republication of Dr. Atkins' *New Diet Revolution*, represents the lowest carbohydrate diet. The Zone diet, also low-carbohydrate, focuses on a 40:30:30 ratio of carbohydrates to protein to fat, a balance said to minimize fat storage and hunger. The LEARN (Lifestyle, Exercise, Attitudes, Relationships and Nutrition) diet follows national guidelines reflected in the U.S. Department of Agriculture's food pyramid-low in fat and high in carbohydrates. The Ornish diet, based on bestsell-

er *Eat More, Weigh Less* by Dean Ornish, is very high in carbohydrates and extremely low in fat.

Study participants in all four groups attended weekly diet classes for the first eight weeks of the study and each received a book outlining the specific diet to which they were assigned. For the remaining 10 months of the study, the women's weight and metabolism were regularly checked, and random phone calls monitored what they were eating.

One of the strengths of the \$2 million study was that this setup mimicked real-world conditions, Gardner said. Women in the study had to prepare or buy all their own meals, and not everyone followed the diets exactly as the books laid out, just as in real life.

At the end of a year, the 77 women assigned to the Atkins group had lost an average of 10.4 pounds. Those assigned to LEARN lost 5.7 pounds, the Ornish followers lost 4.8 pounds and women on the Zone lost 3.5 pounds, on average. In all four groups, however, some participants lost up to 30 pounds.

After 12 months, women following the Atkins diet, relative to at least one of the other groups, had larger decreases in body mass index, triglycerides and blood pressure; their high-density lipoprotein, the good kind of cholesterol, increased more than the women on the other diets.

Gardner has several ideas for why the Atkins diet had the overall best results. The first is the simplicity of the diet. “It's a very simple message,” he said. “Get rid of all refined carbohydrates to lose weight.” This message directly targets a major concern with the American diet right now—the increasing consumption of refined sugars in many forms, such as high-fructose corn syrup.

Beyond pinpointing this high sugar intake, the Atkins diet does the best at encouraging people to drink more water, said Gardner. And when people replace sweetened beverages with water, they don't generally eat more food; they



Christopher Gardner, PhD

simply consume fewer calories over the course of the day.

The third theory Gardner offered as to why the Atkins diet was more successful is that it is not just a low-carbohydrate diet, but also a higher protein diet. “Protein is more satiating than carbohydrates or fats, which may have helped those in the Atkins group to eat less without feeling hungry,” he said.

Although the Atkins group led in terms of the average number of pounds lost, this group also gained back more weight in the second half of the study than those in the three other groups. Gardner also noted that the women in the Atkins group had lost an average of almost 13 pounds after six months, but ended the one-year period with a final overall average loss of 10 pounds.

Though critics of low-carbohydrate diets say that such diets can lead to health problems, none of the factors measured in this study was worse for the Atkins group. Gardner cautions, however, that there are potential long-term health problems that could not have been identified in a 12-month study. Also, several basic vitamins and minerals can be difficult to get in adequate amounts from a very-low-carbohydrate diet.

In the long run, Gardner hopes to use the large data set generated in this study to investigate why different diets might work better for different people. “We’re trying to see if we can learn more about the factors that predict success and failure with weight loss,” he said.

Regardless of what new insights are revealed, Gardner said the message he hopes people take from the study is the importance of eliminating from their diet, as much as possible, refined carbohydrates such as white bread and soda.

Gardner’s co-authors were Alexandre Kiazand, MD, postdoctoral scholar; Sofiya Alhassan, PhD, postdoctoral scholar; Soowon Kim, PhD, data analyst; Randall Stafford, MD, PhD, associate professor of medicine; Raymond Balise, PhD, statistical programmer; Helena Kraemer, PhD, professor of biostatistics; and Abby King, PhD, professor of health research and policy and of medicine.

The work was supported by the National Institutes of Health, and a grant from the Community Foundation for Southeast Michigan.



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breast cancer gene mutation

More Common in Hispanic, Young Black Women, Stanford/NCCC Study Finds

By Amy Adams

A genetic mutation already known to be more common in Ashkenazi Jewish breast cancer patients is also prevalent in Hispanic and young African-American women with breast cancer, according to one of the largest, multiracial studies of the mutation to date.

Researchers at the Stanford University School of Medicine and the Northern California Cancer Center reported the finding from a study of 3,181 breast cancer patients in Northern California. It revealed that although Ashkenazi Jewish women with breast cancer had the highest rate of the BRCA1 mutation at 8.3 percent, Hispanic women with breast cancer were next most likely, with a rate of 3.5 percent. Non-Hispanic whites with breast cancer showed a 2.2 percent rate, followed by 1.3 percent of African-American women of all ages and 0.5 percent in Asian-American women. Of the African-American breast cancer patients under age 35, 16.7 percent had the mutation.

The work, published in the Dec. 26 issue of the *Journal of the American Medical Association*, marks the largest study to date to look at the prevalence of BRCA1 mutations among patients in the four ethnic and racial groups, said lead author Esther John, PhD, research scientist at the Northern California Cancer Center and consulting associate professor of health research and policy at Stanford.

The information could help doctors decide which patients to refer to genetic counseling, the researchers said. They added that they hope the information prompts genetic counselors to develop materials for discussing breast cancer risk in a culturally sensitive way and in languages other than English.

"If a woman has breast cancer she may ask the question, 'Could I be a carrier for a BRCA1 mutation? If I am, my daughters and sons need to know it,'" said senior author Alice Whittemore,

PhD, professor of health research and policy at Stanford. She said that until now, doctors knew only that Ashkenazi Jewish women were more likely to carry a mutation, and therefore frequently referred these women to genetic counseling. What they didn't know is how women of different ethnic groups needed to be treated in terms of their BRCA1 status.

"Traditionally studies have focused on white women," said John. "There is a great need to study racial minorities in the United States."

The risk of a woman developing breast cancer sometime during her life is about one in eight. Although death rates from the disease are dropping, the American Cancer Society estimates that 40,000 women will die from the disease this year.

All people have the BRCA1 gene, which makes a protein that helps the cell repair its DNA. Women who inherit a mutation in that gene from either parent are less able to fix DNA damage and tend to accumulate mutations that lead to cancer. They have a roughly 65 percent risk of developing breast cancer and 39 percent risk of ovarian cancer. If one family member tests positive for a mutation, it can alert other women in the family to also get tested and to take preventive measures.

Without the information from this study, doctors have treated all women other than Ashkenazi Jews as having the same risk level for the mutation. Now doctors who see Hispanic or young African-American breast cancer patients have more information to guide their decisions about referring those women to genetic counseling or testing.

"The message is that these minority breast cancer patients may need screening in ways that we hadn't appreciated before," Whittemore said. She noted that Hispanic women in Northern California, where this study was conducted, derive from different countries than Hispanic women from the East Coast. For that reason, the find-





Shown at far right, researchers Esther John, PhD and Alice Whittemore, PhD.

ings may not apply to Hispanic people in other parts of the country.

John and Whittemore, who are both also members of the Stanford Cancer Center, found a few other surprises in the data. One is that although mutations can occur throughout the BRCA1 gene, the Hispanic women in the study were more likely to carry a particular mutation that's also common in Ashkenazi Jewish women. Other ethnic groups carried a wide range of different mutations.

John and Whittemore think the Hispanic women may have this mutation because of their Spanish ancestry. Spain was the home of Sephardic Jews who could have shared the mutation with Ashkenazi Jews of Eastern European origin.

The prevalence of the mutation in young African-American women with breast cancer also came as a surprise, given that the rate is low in the overall African-American population. The researchers say the finding is consistent with a

long-known pattern that when young African-American women get breast cancer it tends to be a particularly aggressive form of the disease, which is a hallmark of tumors that arise from BRCA1 mutations. Whittemore said this information doesn't change how doctors treat those tumors, but it could help prompt more doctors to recommend genetic counseling for those young African-American breast cancer patients.

Other Stanford researchers who participated in this study include Gail Gong, PhD, a research associate; Anna Felberg, a programmer in health research and policy; Dee West, PhD, professor of health research and policy at Stanford and chief scientific officer at the Northern California Cancer Center, and Amanda Phipps, epidemiologist at the NCCC.

The work was funded by the National Cancer Institute. Reprinted with permission from the Office of Communication & Public Affairs.

cooperative ovarian cancer group for immunotherapy



Dr. Jonathan Berek

The Cooperative Ovarian Cancer Group for Immunotherapy (COGI), based at Stanford University, is a consortium of ovarian cancer researchers from 22 leading academic medical centers throughout the United States and United Kingdom, including Stanford University, Harvard University, Memorial Sloan Kettering Cancer Center, University of Pennsylvania, and the University of Washington. This group was formed in 2004 to focus on the development of vaccines and innovative immunotherapies for ovarian cancer.

Ten institutions are full COGI members and 29 institutions are affiliates. Since its inception, COGI has met annually as a group to plan strategy, and has supported laboratory programs, each of which will initiate a clinical vaccine trial directed for ovarian cancer.

The overall strategy and aims of COGI are to:

- 1) Develop a strong Core Program that coordinates a network of clinical investigators who are dedicated to the conduct of innovative

clinical trials of vaccines and immunotherapies in ovarian cancer.

- 2) Support and facilitate basic laboratory investigations that are designed to translate to clinical trials of ovarian cancer vaccines.
- 3) Create partnerships with biotech industry that will support and utilize our group to conduct meaningful trials and perform correlative assays to study the mechanism of action of the therapies.
- 4) Recruit additional funding to expand our programs and to enable sustained funding beyond our granting period.

COGI is led by group principal investigator, Dr. Jonathan Berek, Professor and Chair, Department of Obstetrics and Gynecology, Stanford University School of Medicine, and the Division of Gynecologic Oncology, Stanford Cancer Center. Central management of this organization is performed by Stanford University personnel, led by COGI Program Coordinator, Colleen Fitzsimmons.



Profile of COGI founder and principal investigator, Jonathan Berek

Jonathan Berek, MD, MMS is an internationally recognized academic leader with special expertise in gynecologic oncology and is the co-editor of the major textbook in this field, "Practical Gynecological Oncology." In addition, the Berek and Novak edition of "Gynecology" is also in press. He is a highly regarded physician, clinical investigator, educator and administrator and has won the praise and respect of colleagues around the world.

Dr. Berek, professor and chair of the Department of Obstetrics and Gynecology and Co-Director of the Women's Cancer Program at the Stanford Cancer Center, was recently elected president of the International Gynecological Cancer Society for three years, 2008-10. The society is the world's largest group dedicated to research and treatment of gynecologic malignancies. Dr. Berek was also elected to the Commission on Cancer of the American College of Surgeons for a three-year term. The commission is a consortium of professional organizations dedicated to improving survival and quality of life for cancer patients through standard-setting, prevention, research, education and monitoring the comprehensive quality of care.

Prior to coming to Stanford in late 2005, Dr. Berek was Vice Chair of the Department of Obstetrics & Gynecology at UCLA. His academic background includes a medical degree from Johns Hopkins; internship and residency at Harvard; and a fellowship at UCLA.

His efforts to create and orchestrate leading ovarian cancer researchers via the COGI consortium promotes optimism that significant gains in the treatment and prevention of ovarian cancer may some day be realized.

women's health in the news

Stanford faculty continue to lead the way in women's health scientific discoveries and new, improved ways of treating patients.


To keep you informed of such developments – along with the ability to see selected women's health seminar presentations on video – a Women's Health “In the News” section can be found on our home page: <http://womenshealth.stanford.edu>.

Most articles identified at the site have been prepared by the Office of Communications and Public Affairs. Videos have been produced by the Women's Health program, often in conjunction with Stanford's Information Resources and Technology group. Some of the videos are also available on Stanford iTunes U (<http://itunes.stanford.edu/>).

Examples of the variety of news features that have occurred in the past two years:

- Stem cell transplant can grow new immune system in certain mice, Stanford researchers find. This represents a step toward creating enhanced immune systems for patients with autoimmune (afflicting women at much higher rates than men) or genetic blood diseases.
- Support groups improve quality of life, but do not extend survival of metastatic breast cancer patients, according to Stanford research team led by David Spiegel, MD.
- Estrogen use lowered one risk factor for heart disease among some younger postmenopausal women, Stanford's Marcia Stefanich, PhD indicates.
- One-visit screening, prevention for cervical cancer holds promise for women in developing countries, Stanford researcher Paul Blumenthal, MD, MPH finds.
- Trastuzumab (Herceptin®) is cost-effective when used after surgery for early HER2-positive breast cancer, indicates Allison Kurian, MD, MSc.
- Few women are consulting their doctors before opting to use herbal therapies and soy products to treat their menopausal symptoms.
- Study closes in on genes possibly linked to depression. Depressive disorders afflict women about 2-3 times more than men.
- Stanford Pediatric/Adolescent Eating Disorder Studies Published. A majority (90%) of pediatric/adolescent patients seeking clinical treatment for eating disorders are female.
- Molecule Linked to Autoimmune Disease Relapses Identified at Stanford. Autoimmune diseases, such as multiple sclerosis, lupus and rheumatoid arthritis, afflict women about 3-times more often than men.
- Face-Lifts: Problems with Deteriorating Facial Bones are More Severe in Women than in Men.
- Cancer Drug May be Potential Remedy for Rheumatoid Arthritis, Stanford Study Finds.
- Stanford Researcher Links Hot Flashes to Insomnia.
- New Osteoporosis Medication Not Cost-Effective Compared With Older, Cheaper Drug, Stanford Study Finds.
- Interview with Former Head of FDA Office of Women's Health . . . Politics v. Science.
- No Link Between Estrogen-Only Therapy, Breast Cancer in Postmenopausal Women.





abuse and assault: a national health crisis for women (that nobody talks about)

*by Harise Stein, MD
Co-Chair, Stanford Medical Center Family
Abuse Prevention Council*

Lauren is a 34 year old engineer. She's in her car, on her way to get a repeat pap smear. She's cancelled twice before because she was just too busy, and has been irritable all day at having to take the time for this appointment. After she gets to her doctor's office, she's surprised at how angry she feels at the receptionist for mispronouncing her name. Then, when she's placed in the exam room and changes her clothes, she starts to feel very anxious. She hates these exams. They always hurt, no matter what the doctor says or does. What women have to go through! While the pap smear is being taken, she grinds her teeth and clenches her hands together, thinking how she just can't wait to get out of there. After she leaves and goes home to make dinner, instead of a sense of relief that the exam is over, she just feels jumpy. She is out of sorts with her boyfriend, and picks a fight over nothing.

Lauren does not realize that a sexual assault she experienced as a teenager, about which she never told anyone, is impacting her ability to take care of her health.

While we would ideally want everyone to live their lives within safe and loving relationships, that is not the case for a large portion of our nation's women. We believe that during their lifetime at least 1 in 4 women will find themselves in an abusive relationship, 1 in 6 will be raped, and 1 in 12 will be stalked (which may include physical or sexual assault). Abuse is found in all demographic groups studied, with no regard to age, race, ethnicity, religion, marital state, sexual orientation, education or socioeconomic status. These experiences may have lasting effects not only on a woman's mental and physical health, but also on how she interacts with healthcare professionals and the medical system.

Trust

Twelve to twenty-five percent of female children in America experience sexual abuse, usually by a family member. In addition, some girls may tell someone about the abuse who either does not believe them, or who chooses to ignore what they have been told. When a child is abused or not protected by someone who is supposed to care for her, she learns to not trust others. As an adult, this difficulty with trust can apply to a variety of relationships, including healthcare providers.

Reminders in the healthcare setting

For some people, coming to the hospital is associated with a sense of vulnerability. This vulnerability is heightened for women with a history of abuse, and is emphasized by being undressed, often lying down, and having intimate areas examined. Women may experience “flashbacks” of past abuse during a variety of medical events, such as breast, pelvic or dental examinations, mammography, vaginal ultrasonography, medical procedures which restrict movement, such as surgery, and during childbirth. As an example, in one small study a group of 44 adult survivors of childhood sexual abuse were surveyed about their experience of having a routine pelvic exam. Sixty-two percent were overwhelmed by emotion, 44% had unwanted or intrusive thoughts, 45% experienced triggered memories, and 55% felt detached from their bodies. One woman felt unable to go back to work for the rest of the day.

Some women may even qualify for a diagnosis of post traumatic stress disorder (PTSD). PTSD may occur months or years after the violent or threatening event, is cumulative with repeat events, and is more common and lasts longer in women than in men.

Appointments and medical decision making

Women may cancel or not show for appointments because of the abuse-related anxiety they experience with certain examinations or procedures. They may also put off needed tests, dental care, or surgery because their anxiety overshadows their medical needs.

What can a woman with an abuse history do?

- Consider whether past abuse experiences are influencing how you manage your healthcare needs.
- Might you have PTSD? (See sidebar.)
- Confide in your healthcare professionals that you are having difficulties, and ask for their support.
- Contact national or local community organizations or clinics, who can provide or refer you to individual or group counseling. (See sidebar.)

What is Stanford Medical Center doing about this issue?

Last year, Stanford Medical Center created a Family Abuse Prevention Council (FAPC). This council is made up of a variety of members from Stanford Hospital and Clinics, the Lucile Packard Children’s Hospital, and the Stanford School of Medicine. As one of its projects, the council has been instrumental in significantly increasing abuse education of medical students, nurses, and all hospital and clinic staff, to compassionately respond to and care for patients who have been or are being abused. To find out more about the activities of the council, contact Dr. Harise Stein (harise@stanford.edu), adjunct clinical faculty member of the department of obstetrics & gynecology, and co-chair of FAPC.

PRIMARY CARE PTSD SCREEN

In your life, have you ever had any experience that was so frightening, horrible, or upsetting that, in the past month, you:

1 Have had nightmares about it or thought about it when you did not want to?

YES NO

2 Tried hard not to think about it or went out of your way to avoid situations that reminded you of it?

YES NO

3 Were constantly on guard, watchful, or easily startled?

YES NO

4 Felt numb or detached from others, activities, or your surroundings?

YES NO

Screen considered positive if you answer yes to three or more items.

Note: A screening technique like this is NOT a definite diagnosis. If you think you might have PTSD, please contact your physician or a mental health care professional.

NATIONAL HOTLINES

National Sexual Assault Hotline
1-800-656-HOPE (4673)
<http://www.rainn.org>

National Domestic Violence Hotline
1-800-799-SAFE (7233)
<http://www.ndvh.org>

National Stalking Resource
Center Hotline
1-800-FYI-CALL (394-2255)
<http://www.ncvc.org/src>

National Center for PTSD
<http://www.ncptsd.va.gov>

Stanford Psychiatry
and Behavioral Sciences Department
650-498-9111

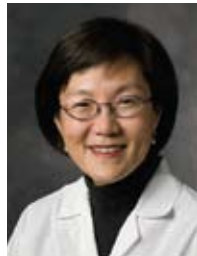
urogynecology

Stanford faculty physicians Bertha Chen, MD and Eric Sokol, MD lead the Urogynecology and Pelvic Reconstructive Surgery Program.

Dr. Chen, an Associate Professor of Obstetrics & Gynecology, received her undergraduate degree from the University of California – Berkeley; graduated from Stanford University Medical School; and completed her internship and residency training at Stanford, as well.

Dr. Sokol, Assistant Professor of Obstetrics & Gynecology, received his Bachelor's Degree from the University of Michigan; completed medical school at Wayne State University, Detroit; his residency at Northwestern University School of Medicine, Chicago; and a fellowship in female pelvic medicine and pelvic reconstructive surgery at Brown University Medical School, Providence.

Both physicians are recognized leaders in the field and possess the clinical and surgical skills, research interest and compassionate values to ensure that their patients' experience is individualized and optimal.



Bertha Chen, MD



Eric Sokol, MD

Program Description

The Stanford Center for Urogynecology and Pelvic Reconstructive Surgery offers cutting-edge diagnostic and treatment options for women with complex pelvic floor disorders such as urinary incontinence, overactive bladder syndromes, pelvic organ prolapse, voiding and defecatory dysfunction, fecal incontinence, fistulas, diverticula and vaginal agenesis. Our center has a particular interest in minimally-invasive, uterine sparing reconstructive surgery for complex pelvic floor disorders.

Our facility includes a new, state-of-the-art urodynamics laboratory and access to a team of specialists, allowing us to offer integrated care to patients in conjunction with pelvic floor physical therapists, urologists, and colorectal surgeons. We also offer consultation for urodynamics testing alone.

The center offers a wide range of state-of-the-art diagnostic and therapeutic procedures as well as consultation services for the following:

- Women with urinary and fecal incontinence
- Women with special problems of pelvic support
- Women who need special reconstructive or reparative pelvic surgery

The center accepts patients for primary management, as well as co-management, thus allowing the referring provider the opportunity to maintain an active role in the patient's care.

Our staff includes subspecialized trained faculty physicians, experienced nurse coordinators, and an administrative assistant who are devoted to the goal of providing the most efficient and highest quality in-house and outreach referral services.



Program Information

Clinical Appointments

650-725-6079
Gynecologic Specialties Clinic
Blake Wilbur Building
900 Blake Wilbur Drive
2nd Floor, W2080
Stanford, CA 94305

Faculty Profiles

Bertha Chen, MD
[http://med.stanford.edu/profiles/
Bertha_Chen/](http://med.stanford.edu/profiles/Bertha_Chen/)

Eric Sokol, MD
[http://med.stanford.edu/profiles/
Eric_Sokol/](http://med.stanford.edu/profiles/Eric_Sokol/)

Physician Referrals

800-756-5000
referral@stanfordmed.org

Clinical Research Studies

[http://womenshealth.stanford.edu/
research/trials/gyn](http://womenshealth.stanford.edu/research/trials/gyn)

Links

Stanford Hospital & Clinics
[http://www.stanfordhospital.com/
clinicsmedServices/clinics/
urogynecology/overview](http://www.stanfordhospital.com/clinicsmedServices/clinics/urogynecology/overview)

American Urogynecology Society
<http://www.augs.org>

Women's Health
<http://womenshealth.stanford.edu>

new monitoring center to provide 'snapshots' of human immune system

By Mitzi Baker

For years, Garry Fathman, MD, and Mark Davis, PhD, dreamed of a place where they could take a sample of blood from a patient and subject it to a battery of tests that would provide a snapshot of that person's immune system. Their dream has come true with the opening of the Human Immune Monitoring Center at the School of Medicine on September 26, 2007.

David Hirschberg, PhD, the director of the center, has set out to realize the vision of every immunologist who ever wondered what was going on with the immune system of a patient.

The center brings together the latest technology for exploring the immune system in one room, in the basement of the Center for Clinical Sciences Research building. Its unassuming appearance belies the enormous undertaking it represents: to provide "one-stop-shopping" for a comprehensive assortment of the most advanced immunological tests available.

"Symbolically, I love being in the basement," said Hirschberg. "This is all about getting in on the ground floor."

The unique facility has a straightforward goal: to run as many tests as possible on one sample—such as a vial of blood—to extract the most information from the least amount of material. Results are integrated to capture an immunological "snapshot" of a person.

That integration is what sets the Stanford center apart from other clinical immunology labs, said Hirschberg. A hospital lab typically would run only one or two specialized tests. Research labs might run any of a number of specific tests to measure immune function. But until now, nobody has put it all together to paint a detailed picture of overall immune system functioning.

"I was brought in to shake things up, to get people to work together, including engineers, industry and clinicians," said Hirschberg, who

On Wednesday, January 23, 2008, David Hirschberg, PhD, director of Stanford's new Human Immune Monitoring Center, spoke to women's health medical colleagues, giving a talk titled: Stanford's Human Immune System Monitoring Center: Implications for the Health of Women. This center is a significant example of how Stanford researchers are working together to make discoveries that can be translated into improved medical care, including the many autoimmune diseases (where women are afflicted at much higher rates).



came from a Silicon Valley company, Agilent Technologies, after his postdoctoral fellowship at Stanford.

Even before Hirschberg's group moved to their new basement digs, they had been functional for the past six months. A number of collaborative studies have already begun—with researchers from Stanford, as well as from other institutions—including investigations of immune system involvement in atrial fibrillation, chronic fatigue syndrome, hepatitis C, juvenile rheumatoid arthritis, tuberculosis and prostate cancer.

Ian Lipkin, MD, a professor of neurology and pathology from Columbia University, has been using the services to study what goes wrong with the immune system in autism. "Analyses of serum from children with autism has already yielded important insights that have implications for early diagnosis and management," said Lipkin. "The Human Immune Monitoring Center is an extraordinary resource for Stanford and the larger scientific community."

Funded by a \$1.5 million gift from the HEDCO Foundation for the equipment, in addition to grants from the Russell Foundation, the Sidney Frank Foundation and the Becton Dickinson Corp., the small room may hold the answer to many of the mysteries of the immune system.

The lab provides a dozen different tests, including genetic analysis and cell sorting that can pick out extremely rare immune cells from a blood sample. The center is also establishing

its own database so that so that researchers can survey across the many different diseases with immunological components to look for similarities and differences.

"This center is the first of its kind," said Fathman, who is a professor of medicine and director of the Center for Clinical Immunology at Stanford. He emphasized that the center will document the range of what is "normal" immune function. "What we want to create is the roadmap for normalcy," he said, which can be used as a reference for studying immune dysfunction.

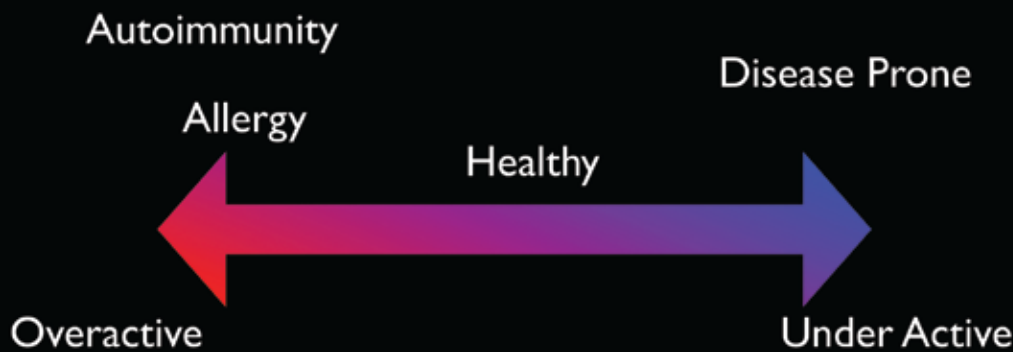
"If I go to my doctor and ask, 'How is my immune system doing today,' I would probably get a blank stare," said Davis, professor of microbiology and immunology and director of the Institute for Immunity, Transplantation and Infection."

Much like doctors routinely test for blood lipids now, the founders of the immune monitoring center want to create parallel standards for the immune system. "We want to be predictive," Davis said.

"This will be of immediate benefit to the study of some diseases, but getting to the 'big picture' will take some time and a lot of hard and intensely collaborative work," said Davis. "But in five to 10 years this could really change the face of medicine."

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The Immunological Spectrum



making an appointment stanford university medical center

Stanford Hospital & Clinics

www.stanfordhospital.com/default

To request an outpatient clinic appointment at Stanford Hospital & Clinics, you may:

- New patients, please contact the Stanford Referral Center, where our staff can help you access physicians and medical services at Stanford Hospital & Clinics. You can reach the Stanford Referral Center by email at referral@stanfordmed.org, or by calling (800)756-9000.
- Cancer patients can call (877) 668-7535.
- For established patients, please call the clinic directly. Clinic phone numbers can be found at: <http://www.stanfordhospital.com/clinicsmedServices/default>.
- For International patients, please contact International Medical Services, via email at ims@stanfordmed.org, or by calling 650-723-8561.

Lucile Packard Children's Hospital at Stanford

www.lpch.org

Lucile Packard Children's Hospital is dedicated to the care of babies, children, adolescents, and expectant mothers.

To request an appointment, please contact:

- Packard Children's Hospital Referral Center at referral@lpch.org, or by calling (888) ASK-LPCH (275-5724).
- For find information about individual clinics, please go to: <http://www.lpch.org/clinicalSpecialtiesServices/index.html>.

how to find open clinical trials at stanford university medical center

Stanford clinician scientists are engaged in a wide variety of clinical trials investigating new approaches to preventing and treating conditions and diseases. The variety of therapies being studied range from new pharmaceutical drugs and medical devices to behavioral and biotechnology therapies. These trials are done in close collaboration with scientists and physicians from many areas of expertise across Stanford University. To insure the highest ethical standards are maintained the Institutional Review Board (IRB) is responsible for oversight of all studies.

To find out specifics about current clinical trials at Stanford, visit/contact any of these resources:

- master listings of adult and pediatric trials, go online to:
<http://med.stanford.edu/clinicaltrials/home.do>
- for information about all current cancer trials, visit:
<http://cancer.stanford.edu/trials/>
- women's health trials in the department of obstetrics and gynecology,
email womenshealth@stanford.edu or call 650-725-9977

how to contact the women's health program group



Contact information for
Stanford's Women's Health program:

web: <http://womenshealth.stanford.edu>

email: womenshealth@stanford.edu

phone: 650-725-0455

address: 900 Welch Road, Suite 20, Palo Alto, CA 94304

director: Lynn Westphal, MD

executive director: Jim Batterson (jimbat@stanford.edu)

<http://womenshealth.stanford.edu>



Women's Health
STANFORD

900 Welch Road, Suite 20
Palo Alto, CA 94304

<http://womenshealth.stanford.edu>