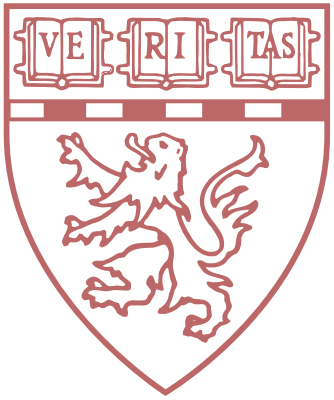
Beth Israel Deaconess Medical Center

A teaching hospital of Harvard Medical School

OBSTETRICS & GYNECOLOGY

2004 **ANNUAL REPORT**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MESSAGE FROM THE CHAIR

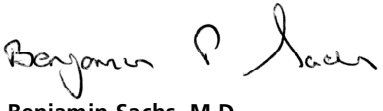
Beth Israel Deaconess Medical Center (BIDMC), a flagship teaching hospital of Harvard Medical School (HMS), is known for its exemplary patient care, leading-edge clinical and basic science research, and outstanding educational programs. The department of obstetrics and gynecology takes great pride in providing cutting-edge care for women, delivered with a personal touch and respect for diversity. As a major teaching hospital of HMS, we offer a residency program in obstetrics and gynecology that consists of 20 residents (5 residents per year). We teach women's health to 40% of HMS students, and I currently chair the Executive Committee for OB/GYN at HMS, a position that rotates among the three major Harvard teaching hospitals. The size of our residency program allows us to have a feeling of smallness and individuality that is partnered with an emphasis on evidenced based medicine and research. Our unique blend of academic rigor, combined with empathic and individualized care, is what makes us unique. We are the "small college" residency experience of HMS.

At BIDMC, our greatest assets are our staff and patients. Our extraordinary group of attending physicians, residents, and medical students work in partnership with our world-renowned nurses. This unique relationship raises our quality of patient care a notch above the rest. Social workers, administrators, support staff, and physicians in our related fields complete the team. Our diverse patient population hails from various ethnic and socioeconomic backgrounds and together we care for all of them. Residents participate in the care of all patients; hence there is no two-tiered model of care in our department. We care for all patients together, and believe that it takes a team effort to deliver safe and excellent health care.

In addition to serving our patients, the medical center is committed to being active in our local community. Service to community is at the core of the religious tradition of both of our founding hospitals, and an important part of our mission. We have a covenant to care for the underserved and to work to change disparities in access to care. We know that to be successful we need to learn from those we serve.

The department of obstetrics and gynecology at BIDMC is seeking resident applicants who choose to make a difference. We are not looking for one uniform type of individual, but rather are seeking those with passion. Our residency training program prepares future obstetrician/gynecologists for a myriad of opportunities - research, public health, education, or clinical medicine. We seek to develop future leaders. In a continuing effort to improve resident education and patient care, BIDMC and the department of obstetrics and gynecology are fully committed to the national resident work hour guidelines. If you want to make a difference and you have the passion, please join us.

We recognize that the diversity, talent, innovation, and commitment of all of our employees contribute to our strength and are a major component of our success. We greatly value the leadership and participation of our trustees, overseers, and donors who make an invaluable contribution to our ability to carry out our mission to serve patients, students, science, and our community.



Benjamin Sachs, M.D.

Harold H. Rosenfield Professor, Harvard Medical School
Professor, Harvard School of Public Health
Chief Obstetrics, Gynecology and Reproductive Biology

Department of Obstetrics and Gynecology

The department of obstetrics and gynecology provides comprehensive, compassionate, integrated healthcare to women of diverse backgrounds. Services include preventive women's healthcare, reproductive endocrinology and fertility treatment, low and high-risk pregnancy care, operative gynecology, menopause and geriatric women's health care, and cancer care for women. The department's goal is to approach life-cycle events with a combination of holistic care and state-of-the-art medical intervention. Program staff includes physicians, nurses, nurse practitioners, social workers, and many other individuals who work collaboratively to provide care. Interns, residents and medical students work under the direct supervision of an attending physician.

Beth Israel Deaconess Medical Center

A major teaching affiliate of Harvard Medical School (HMS), Beth Israel Deaconess Medical Center (BIDMC) is renowned for excellence in patient care, biomedical research, teaching, and community service. Located in the heart of Boston's medical community, it hosts nearly three quarters of a million patient visits annually in and around Boston.

The medical center is renowned for excellence in surgery (including general, cardiovascular, thoracic, gastrointestinal, solid organ transplant and vascular surgery), with minimally invasive approaches to many procedures and obstetrics and women's health. BIDMC is also known for treatment of cardiac conditions, cancer, and pulmonary and thoracic disorders; and for our expertise in neurosciences, gastroenterdology and liver disease, podiatry, and emergency and trauma medicine.

BIDMC provides an exceptionally caring environment for patients and families, especially through its "heart and soul" programs - geriatric care, social work, palliative care and affiliated community health centers.

Harvard Medical School

Established in 1782, the Harvard Medical School mission is to create and nurture a community of the best people committed to leadership in alleviating human suffering caused by disease. Under the leadership of Dean Joseph B. Martin, M.D., Ph.D., HMS attracts the best and brightest students. The class of 2007 represents a distillation of the hopes and aspirations of a substantial number of Americans. More than 5,300 students aspired to enter HMS in the fall of 2004, resulting in a class numbering 165. Each student was selected on the basis of many achievements in life to have a special spark of creativity or broad interest that will make them the leaders of tomorrow, whether in the art or the science of medicine.

Beth Israel Deaconess Medical Center Achievements

1922 – The first administration of insulin in New England occurred at Deaconess Hospital

1960 – The first implantable cardiac pacemaker was developed at Beth Israel Hospital

1972 – The first Rights of Patients statement in the nation implemented at Beth Israel Hospital

1983 – The first successful liver transplant in New England was performed at the Deaconess Hospital

1986 – The first baby conceived through in vitro fertilization in Massachusetts was delivered at Beth Israel Hospital

1991 – The first evidence that abnormalities in the visual system of the brain could help explain problems of people with dyslexia was discovered by Beth Israel researchers

1995 – New England's first minimally invasive coronary bypass surgery was performed at Deaconess Hospital

1995 – The first deep brain stimulator implantation for the treatment of Parkinson's disease in New England was performed at Deaconess Hospital

1998 – Beth Israel Deaconess Medical Center performed the first adult live-donor liver transplant in New England

1998 – A patent was issued for the Cohn cardiac stabilizer, developed by Beth Israel Deaconess Medical Center cardiothoracic surgeon William Cohn, M.D., allowing coronary artery bypass surgery to be performed without the use of a heart-lung machine

2002 – Beth Israel Deaconess Medical Center became the only clinical trial site in Boston to test a new therapeutic AIDS vaccine on normal, healthy adults

2003 – BIDMC researchers discovered the probable cause of preeclampsia — *Published in The New England Journal of Medicine and The Journal of Clinical Investigation*

2003 – Beth Israel Deaconess Medical Center joined a select list of hospitals nationally conducting the first clinical trial of the AbioCor® Implantable Replacement Heart

RESIDENCY TRAINING IN OBSTETRICS AND GYNECOLOGY

Hope A. Ricciotti, M.D.
Director of Medical Education, Residency Program Co-director

Young Bae Kim, M.D.
Residency Program Co-director

The Beth Israel Deaconess Medical Center (BIDMC) residency program in obstetrics and gynecology consists of 20 residents (5 residents per year). Our principal clinical site is BIDMC, which is adjacent to the Harvard Medical School (HMS) campus in the Longwood Medical area. Several rotations occur in outside sites, including Mt. Auburn Hospital in Cambridge, and Metrowest Medical Center in Framingham.

PGY 1

- Surgery
- Medicine
- Emergency medicine
- Ambulatory obstetrics & gynecology
- Ultrasound
- Obstetrics
- Gynecology

PGY 2

- Obstetrics
- Gynecologic oncology
- Reproductive endocrinology
- High-risk obstetrics
- Elective / Research

PGY 3

- Gynecology
- Advanced urogynecology and gynecologic laparoscopy at Mt. Auburn Hospital
- Gynecology at Metrowest Medical Center
- High-risk obstetrics
- Obstetrics rotation
- Elective/Research

PGY 4

- Obstetrics chief
- Gynecological chief
- Oncology chief
- Clinic chief
- Swing chief

ELECTIVE AND RESEARCH

Research and academic pursuits by residents are highly valued and supported in the department of obstetrics and gynecology. Residents are strongly encouraged to formulate research ideas and seek preceptorship for projects upon entry as a PGY1. Residents may perform basic science research, clinical research, educational research, international health care projects, or any approved creative academic pursuit. Residents may work with faculty in the department of obstetrics and gynecology, BIDMC, or HMS.

In the post-graduate years two and three, time is allotted for elective and research rotations. Residents are encouraged to publish their completed work and to present it at national meetings. Financial support is provided by the department of obstetrics and gynecology for residents to travel to meetings when projects are accepted for publication or presentation. Up to $1,000 may be granted for travel and expenses. Financial assistance is available for laboratory supplies, materials, statistical analysis, etc.

Recent research/elective projects have included clinical investigations in infertility, evaluations of medical errors, evaluation of educational teaching techniques, basic science investigations in reproductive endocrinology, international health projects in third world countries, and web-based educational projects.

FORMAL TEACHING

Grand Rounds

Grand rounds is a weekly, one-hour program orchestrated by Dr. Johanna Perlmutter. It consists of lectures by invited guest speakers, named lectureships, chief resident presentations, and monthly complications review and management conference. A broad range of topics ranging from preventive medicine, cutting-edge research, advanced clinical topics, and education are presented in a formal setting attended by all faculty, residents, nursing leaders, and administrators in the department of obstetrics and gynecology.

Resident Didactic Series

Residents participate in a didactic series of lectures and tutorials in obstetrics, gynecology, and women's health for two hours each week. The topics cover the broad range of learning objectives and competencies necessary to achieve proficiency in the field of obstetrics and gynecology. Attendees include residents and medical students. The residents have no clinical responsibilities during these teaching sessions.

Perinatology Conference

Perinatology conference is a weekly interdisciplinary one-hour seminar conducted by the faculty of the divisions of maternal-fetal medicine, anesthesia, internal medicine, and neonatology. The chief obstetrical resident is responsible for organizing this conference. Presentations and discussions are case-oriented and focus on current complex clinical issues managed by the maternal-fetal medicine service. Attendees include medical students, residents, faculty, nursing, and social service workers. Representatives from a number of consultative services attend regularly to contribute special expertise in genetics, radiology, endocrinology, hematology, cardiology, nephrology, and infectious diseases.

High-Risk Clinic Review Conference

One-hour per week is devoted to a formal review of the progress and management plans for patients on the obstetrical high-risk ambulatory service. A maternal-fetal medicine specialist reviews cases with the obstetrical team, and care plans are outlined for each patient. Attendees include residents, medical students, social services, and nursing.

Gynecologic Tumor Board

The Gynecologic Tumor Board meets weekly under the direction of the faculty of the gynecologic oncology division. This multidisciplinary conference includes faculty from medical oncology, radiation therapy, and pathology. All current gynecologic cancer cases are reviewed in detail for interdisciplinary treatment planning. Cases are considered in advance of definitive therapy to ensure full evaluation, suitable consultation and uniformly structured care with follow-up. The oncology resident service members are required to attend.

Obstetrics & Gynecology Morbidity and Mortality Conference

Morbidity and mortality conference is a bi-weekly conference devoted to a discussion of all complicated cases that have occurred in our department in the preceding weeks. Residents who participated in the medical management present cases and include a review of the pertinent medical literature. Division directors are present at this meeting to add clinical and academic expertise and evidence-based guidance to the discussion. Attendees include residents and medical students.

Maternal-Fetal Medicine Rounds

Morning rounds are conducted each day on the obstetrics service under the leadership of the obstetrics chief resident. The maternal-fetal medicine attending on service supervises these rounds, offering insights and evidence-based guidance into management. Literature reviews, resident and medical student presentations, and educational discussions are part of these patient care conferences. Attendees include residents and medical students on the obstetrics service. This is followed by "board rounds" to review patients present on the labor and delivery ward at the start of the day.

Gynecology Rounds

Morning rounds are conducted each day on the gynecology service under the leadership of the gynecology chief resident. These are supervised by the gynecology attending on service, who offers additional insights and evidence-based guidance into management. Literature reviews, resident and medical student presentations, and educational discussions are part of these patient care conferences. Attendees include residents and medical students on the gynecology service.

Journal Club

A monthly journal club facilitates the critical review of current obstetric and gynecologic literature. Dr. Bruce Cohen (maternal-fetal medicine), Dr. Steven Bayer (reproductive endocrinology), and Dr. Young Kim (gynecologic oncology) orchestrate this literature review. Articles are submitted for review by faculty and residents. Three articles are chosen and briefly reviewed, first by a resident and then by faculty, who offer interpretation. Techniques for journal review, statistical analysis, and clarity of presentation are stressed. In addition, OB/GYN faculty and epidemiologist, Dr. Marlene Goldman, performs an in-depth review of one scientific publication each month.

Reproductive Endocrine Case Conference

A weekly reproductive endocrine conference serves to provide an in-depth discussion of patients with endocrine or menstrual issues. Residents and the clinical fellows in reproductive endocrinology prepare patient presentations. In addition, a short unknown case of the week is presented, in which a 35mm slide (unknown to fellows and residents) is shown for discussion. The conference also includes a series of endocrine faculty lectures, which cover basic topics of reproductive endocrinology and infertility. Attendees include reproductive endocrine faculty, fellows, residents, and medical students.

Resident Teaching Workshop

Three times per year, a two-hour resident-teaching workshop is conducted. These feature one-on-one faculty and resident interactions focused around a specific skill, area of knowledge, or focused clinical experience. Workshop topics are targeted toward different resident levels and may include case-based teaching topics, critical care simulated cases, resident as teacher modules, and surgical skills simulation, such as laparoscopy and laser.

Resident Laparoscopic Education Program

The BIDMC residency program offers a structured laparoscopic laboratory and training program as part of the formal resident teaching series. The medical center houses a Technical Skills and Simulation Lab, in which surgeons and residents from BIDMC gain proficiency in basic and advanced laparoscopic procedures. Featuring a number of different and sophisticated simulators, like those used in flight aviation, the lab offers benchmark training and research opportunities to prepare the next generation of laparoscopic surgeons.

Under the supervision of Dr. Sandra Dayaratna, the goal of the OB/GYN laparoscopic education program is to improve residents' skills, speed and proficiency in laparoscopic techniques in a skills laboratory, in order to maximize the clinical surgical experience. Residents use simulated surgical techniques with alphabet pieces, coffee beans, strings, and other devices in order to improve surgical proficiency in minimally invasive techniques.

AMBULATORY RESIDENT PRACTICE

Ronald Marcus, M.D.
Director

Women's Health Associates is the resident ambulatory practice in obstetrics and gynecology at BIDMC. Housed in the state-of-the-art Shapiro Clinical Center, it is an academic setting in which house officers are closely supervised by faculty preceptors, yet ownership and longitudinal care of each resident's panel of patients are encouraged. Our goal is for the residents to provide quality ambulatory care to patients in a warm, non-threatening environment. An integrated health care team provides women of diverse backgrounds with the full gamut of general and specialized obstetric and gynecologic care. This team includes physicians, nurse practitioners, R.N.s, social workers, nutritionists, counselors and patient advocates.

Residents participate actively on a continuous longitudinal basis, performing one weekly half-day ambulatory session, regardless of their other assigned hospital service functions. Throughout the course of their entire training program, residents care for their own panel of patients in consultation with a faculty member. One full-time physician is assigned as preceptor for each session, with the exclusive role of providing supervisory guidance, support and teaching for residents and students. Residents establish long-term doctor-patient relationships and study the evolution and management of pregnancy pathophysiology and gynecologic disease and prevention. Continuity of care is emphasized so that residents are expected to arrange for and participate in all office or hospital treatments and procedures needed by their patients.

Residents are divided into teams, with each team having a specific set of health assistants and nurses, as well as a social worker and attending physician (designated the "team leader"). Regular team meetings ensure patient continuity. The BIDMC computer system is used to track patients and to allow follow-up of laboratory values and other clinically relevant data.

Call

Chief Year	One in five call
PGY1-3 OB	Day and night shift rotations
PGY1-3 GYN	One in four to one in five call

Benefits
BIDMC provides residents with a competitive fringe benefit package that includes health insurance, disability insurance, pension, and professional liability insurance. Membership in multiple on-line journal services and medical information is provided through BIDMC and HMS for all residents.

Research Project Funding
Funding is available from the Department of Obstetrics and Gynecology Research Foundation for costs associated with resident research projects. Funds are approved on a case-by-case basis by a formal review process.

Vacation (annual)
PGY 1 Three weeks
PGY 2-4 Four weeks

Educational Conferences and Meetings
Chief residents are given a stipend to cover expenses to attend one approved professional/educational conference. Up to five additional days off are allotted for conference attendance. There are some rotations during which a conference is not allowed.

Residents who have research projects accepted for presentation may travel to approved conferences. Residents may apply to the BIDMC OB/GYN Foundation, Inc. for funding up to $1,000 to cover expenses for travel.

Harvard Medical School Conferences
All post-graduate and professional conferences sponsored by HMS, regardless of sponsoring medical center, may be attended free of cost by BIDMC residents.

WOMEN'S HEALTH EDUCATION AT HARVARD MEDICAL SCHOOL

Hope A. Ricciotti, M.D.
Director of Medical Education, Co-director, Medical Student Program

Mimi Yum, M.D.
Co-director, Medical Student Program

The department of obstetrics and gynecology at BIDMC plays a leading role in teaching women's health to HMS students. Sex and gender differences in health and disease have been recognized in many fields over the last two decades, creating a significant new body of knowledge that warrants inclusion in medical curricula. Our goal is to ensure that all students, regardless of specialty, are prepared for the challenge of the complex health needs of women, both clinically and in research.

With this in mind, physician educators from our department lead the ongoing effort to incorporate women's health into the Year I and II curriculum at HMS. Our department provides leadership in directing the third year core clerkship in obstetrics and gynecology at the Harvard teaching hospitals. Finally, we offer specialized electives and sub-internships to year IV students in women's health.

Year I and II Curriculum Reform in Women's Health
Physician educators from our department work in partnership with course directors and educators at HMS, in order to ensure the complete incorporation of women's health into the HMS curriculum. The reform process is a continuous and on-going one, which includes regular assessment and integration of important topics in women's health throughout the four-year undergraduate medical curriculum.

Recognition of women's health, as a field requiring a multidisciplinary approach in teaching medical students the specific health issues of women, has led to many changes throughout the HMS curriculum. HMS has historically taken a unique approach to addressing important health issues by incorporating longitudinal themes throughout the four-year curriculum. Curricular themes were developed at HMS as a way to incorporate important material into the curriculum without adding additional courses. Altering the content of existing courses rather than adding additional course work addresses important health issues in a multi-disciplinary fashion at varying levels of student learning.

There are currently ten curricular themes that have been integrated throughout the HMS curriculum; into the lectures and cases taught during the first two years, and the clinical clerkships of years three and four. Under the leadership of physician educators in our department working with the Harvard Center of Excellence in Women's Health, Women's Health was named the tenth curricular theme at HMS in academic year 1999-2000. Since that time, Dr. Hope Ricciotti has served as Women's Health Theme Director. In 2004 she was named the deputy director for education at the Harvard Center of Excellence in Women's Health, a Health and Human Services program of the U.S. Government.

As a result of these efforts, women's health issues are presented to medical students at HMS in a developmentally appropriate way, spanning all four years of medical education. A major goal of this effort is to keep women's health broadly distributed in the curriculum so that the effort is not limited to those who will go into OB/GYN, or to those who see themselves as future "women's health physicians." Rather, all students will learn about women's health and how it may be practiced and incorporated in their particular chosen field.

Core OB/GYN Clerkship

The department of obstetrics and gynecology offers a core OB/GYN clerkship experience for third year HMS students. Approximately one-third of students enrolled at HMS rotate through this clerkship. This course offers a core clerkship experience that aims to approximate the actual delivery of care in women's health. One-third of time is spent in the ambulatory setting, one-third in labor and delivery, and one-third in the gynecologic operating room. Students and residents in OB/GYN at BIDMC are involved with all patients, both private and "clinic". Therefore, students are taught not only by the house staff, but also by faculty and private physicians. This allows for a breadth of experience in types of patients encountered and teaching styles.

The ambulatory experience is based upon a preceptor model in which each student is paired with a general OB/GYN faculty preceptor who directs the outpatient experience. This outpatient experience is longitudinal throughout the clerkship - the student has an ambulatory session once a week with their core preceptor. This maintains continuity in both patient care and the student's own learning under the preceptor's guidance. In addition, students have a weeklong outpatient experience that includes sessions in reproductive endocrinology, maternal fetal medicine, gynecologic oncology, urogynecology, genetics, antenatal testing, and community health.

The labor and delivery experience includes participation in normal deliveries, cesarean deliveries, high-risk obstetrics, and high-risk antepartum care. The gynecologic experience includes participation in general gynecology, gynecologic oncology, and urogynecologic surgery. Students take night call every 4-5 nights on both the obstetrical and the gynecologic services. Faculty gives approximately 3-4 formal teaching presentations per week, which complement the clinical experience so that full curriculum objectives are met. Weekly formal bedside rounds with the department chairman round out the experience. A mid-clerkship lunch with the clerkship directors allows for informal feedback and career counseling.

Drs. Hope Ricciotti and Mimi Yum serve as clerkship co-directors. Dr. Hope Ricciotti serves as the HMS OB/GYN clerkship Committee director, a role in which she ensures common clerkship objectives, evaluation, and grading are performed across clerkship sites. In this role, she serves as liaison between HMS and department chairs from the various teaching sites.

Fourth Year Electives

The department of obstetrics and gynecology offers several advanced electives in women's health to fourth year medical students. These electives are open to both HMS students and selected students from outside institutions.

Sub-internship in obstetrics – Dr. Kee-Hak Lim, a maternal-fetal medicine specialist, serves as course director

Sub-internship in gynecologic oncology - Dr. Young Kim, a gynecologic oncology specialist, serves as course director

Educational Research Projects

Physician educators from the department are active in educational research, evaluating new teaching methods, tools and technology in order to improve teaching methods and lead the larger education community in these methods.

Obstetrical Virtual Patient Project

The virtual patient is a computer simulation tool designed to educate medical students in the skills of patient care. The creation of the virtual patient was funded by the Macy Foundation and authored by a multidisciplinary team from the departments of obstetrics and gynecology, medicine, neonatology, radiology and social services at BIDMC. The lead author is Dr. Hope Ricciotti.

The normal pregnancy virtual patient computer simulation case is based on a female patient during the course of her preconception care, normal pregnancy and postpartum course. It is available on the Mycourses website of HMS and takes approximately one hour for students to complete. It is an interactive, multimedia program that includes audiovisual excerpts from ultrasounds, office visits and labor and delivery.

In the computer simulation program, the student meets the virtual patient when she is contemplating pregnancy. The student follows the virtual patient from preconception care, through the course of a normal antepartum, labor and delivery, and postpartum. This longitudinal experience is not possible in the traditional six-week OB/GYN core clerkship. The student interacts with the virtual patient by answering questions in the computer program that lead the student through the case while they are given feedback on their answers.

In order to assess the effectiveness of the virtual patient computer simulation tool, the BIDMC OB/GYN Foundation, Inc. has funded principal investigator, Dr. Hope Ricciotti, to perform a randomized educational assessment project of the virtual patient. The hypothesis is that students on their OB/GYN clerkship, who have been exposed to the normal pregnancy virtual patient, will have a greater ability to provide preconception, prenatal and postpartum care to a patient. Beginning in academic year 03-04, half of the students rotating through the BIDMC OB/GYN clerkship are randomized to experience the traditional clerkship, and half experience the traditional clerkship plus the normal pregnancy virtual patient.

At the end of the clerkship, students will be asked to volunteer to participate in a simulated patient interview and counseling session. A trained, standardized patient will be used to assess the student's ability to counsel a woman in preconception care, to provide options for genetic counseling, to educate her about breastfeeding, and to screen her for postpartum mood disorders. The session will be videotaped and a physician who is not a faculty member in the clerkship will review the student's performance and answer a checklist of assessment questions. The physician reviewer will be blinded to whether the student has used the virtual patient program.

Resident as Teacher Project

Working in collaboration with the HMS Office of Education, physician educators from the department of obstetrics and gynecology have led the effort to enhance resident teaching of medical students. Dr's. Mimi Yum and Hope Ricciotti lead the program.

The HMS Resident as Teacher Initiative was begun in 1997 as part of a one-year multi-institutional fellowship program supported by the Harvard Macy Institute. The OB/GYN Resident as Teacher Program is a subset of this multi-disciplinary initiative. This program acknowledges the vital role OB/GYN residents play in educating medical students and serves to enhance their teaching skills. OB/GYN is an extremely active discipline in which much teaching and learning is done "on the fly". It is thus essential to maximize these opportunities.

Two major teaching modalities for residents have been developed through this program. First, based on the learning objectives for medical students outlined by the Association of Professors of Gynecology and Obstetrics (APGO), a resident as teacher lecture series has been designed. These lectures focus on the most relevant topics and learning objectives in OB/GYN, using a clinical case study design simulating true teaching opportunities. Guidance is given on how to adequately address the essential teaching points during the course of a busy clinical day.

Second, videotaped simulated teaching encounters have been used to provide feedback on resident teaching skills. These sessions provide residents with the opportunity to pilot their teaching strategies. While being videotaped, a trained medical student volunteer presents a case to the resident. The resident in turn teaches the student the principles illustrated in the case, emphasizing learning objectives throughout the presentation. Subsequently, the resident watches his/her video in private and then returns for immediate feedback on his/her teaching style and tactics.

Resident-Led, Educational Research Projects

- Evaluation project of the effectiveness of the simulated video-taped
  Holly R. Khachadoorian, M.D., M.B.A., Mimi R. Yum, M.D., Hope A. Ricciotti, M.D.
- Creation and evaluation of "Teaching Cards" for enhancement of resident teaching on the fly
  Sadia Hadar M.D., Hope A. Ricciotti, M.D., Mimi R. Yum M.D.

FELLOWSHIP PROGRAM IN REPRODUCTIVE ENDOCRINOLOGY

Richard H. Reindollar, M.D.
Director

Under the direction of Richard H. Reindollar, M.D., the Beth Israel Deaconess Medical Center/Harvard Medical School fellowship training program in reproductive endocrinology and infertility is entering its eighth year. This board-certified three-year fellowship provides comprehensive training with a very broad clinical experience and exposure to cutting-edge basic and outcomes research. Each fellow spends the first eighteen months of this fellowship in the division-based science laboratory, and the second eighteen months in extensive clinical training. During the first year of the clinical experience, concentrated time is spent in rotations, not only with reproductive endocrinologists, but also with other subspecialists such as medical endocrinologists, pediatric endocrinologists and a male infertility specialist.

Boston IVF serves as the clinical component of the fellowship training program. It is the largest in vitro fertilization program in the United States, providing fellows with a unique and extensive clinical experience in all aspects of reproductive care. In addition, the fellows participate in clinical faculty practices that include a number of patients with pure reproductive endocrine problems, ranging from intersex disorders through menstrual abnormalities and menopause. The basic science research is usually performed within the division laboratory at BIDMC. Under the direction of Anny Usheva, Ph.D., this laboratory provides cutting-edge molecular technology training and propels the fellows into separate areas of potentially long-term research. For a number of years, the laboratory has studied the molecular basis of mullerian defects. More recently, it has begun to focus on ovarian aging, both in the mouse model and humans. Studies have been initiated to better understand the recruitment of the dominant follicle. Fellows may also elect to perform their basic research in one of the many laboratories within the HMS system.

Over the past eight years, seven fellows have completed the BIDMC fellowship training program; three of these fellows presently practice within universities, one is in a private practice affiliated with a teaching program, and three are presently in private practice. The last annual report submitted to the American Board of Obstetrics and Gynecology included nine abstracts presented by fellows at annual meetings and the publication of fourteen papers authored by fellows in the previous year. During the past year, faculty presented seven abstracts at annual meetings and published six papers. The research, teaching and clinical experiences provided by this fellowship program have made it one of the most popular and sought after training programs in the country. This past year, more than one hundred fellowship applications were received for the position beginning in July 2005.

GYNECOLOGY

David Chapin, M.D.
Division Director

Mission
The division of clinical gynecology directs integrated, high-quality care to patients with gynecologic disorders.

Clinical Care
All the clinical subspecialties of clinical gynecology are practiced in this department, including urogynecology, minimally invasive surgery and geriatric surgery. Pathophysiologic mechanisms of disease states and rational therapy are emphasized, especially with regard to the type and the proper timing of operative procedures. Principles of pre- and post-operative care principles are stressed. This division directs the Gynecologic Triage Unit, where patients with gynecologic emergencies are seen by residents and staff from our department. This unit allows residents and students to make the initial diagnosis and treatment plans on patients, an increasingly rare opportunity.

Education
Residents are given increasingly greater responsibility for total care of gynecologic patients as they show the capability to accept such responsibility. Technical surgical skill in abdominal and vaginal procedures are taught in a progressive manner over the course of the program, so that residents acquire the full range of skills expected of highly competent practitioners before they complete the program. The case load proves quite sufficient for these purposes because, without exception, every operative procedure done by a member of the faculty of this department is expected to be a learning experience for the residents.

In addition to daily patient management and teaching rounds, bedside and operating theater teaching are carried out on all cases, and there are regular staff and resident conferences held on subject matters of relevance.

GYNECOLOGIC ONCOLOGY

Young B. Kim, M.D.
Division Director

Mission
The division of gynecologic oncology is dedicated to superior clinical care, teaching, and research for women with cancer of the reproductive tract.

Clinical Services
The division of gynecologic oncology conducts an active clinical program for the management of gynecologic cancer. The division works in a multidisciplinary fashion with medical oncologists, radiation oncologists and pathologists in order to optimally treat women with cancer of the reproductive tract. The spectrum of therapeutic options includes surgery (encompassing radical and ultra-radical procedures), radiation, chemotherapy and biological therapies. Clinical outreach programs are currently in operation at Mount Auburn Hospital and Brockton. These programs provide on-site surgical consultation.

COLPOSCOPY AND LASER SURGERY UNIT

Louis Burke, M.D.
Director

The Colposcopy, Laser and Electrosurgery Clinic is a referral clinic for patients with benign and neoplastic problems involving the vulva, vagina, and cervix. Most patients are referred for the evaluation of abnormal Pap smears. Patients who have human papilloma virus and have not responded to the usual modes of therapy are also referred for evaluation and possible treatment with the carbon dioxide laser. A large number of women exposed to diethylstilbestrol (DES) in utero are seen in the clinic. Treatment modalities such as CO2 laser and LLETZ are offered.

Patients with abnormal smears during pregnancy are followed for evidence of developing invasive disease. A large number of patients exposed in utero to diethylstilbestrol are continually being examined and followed utilizing colposcopy. The Large Loop Excision of the Transformation Zone (LLETZ) or carbon dioxide laser is used in most cases as treatment modality, both as an outpatient procedure and in the operating room. Laser ablation, cervical conization, partial vaginectomy, partial vulvectomy and evaporation of condyloma are performed using the carbon dioxide laser, as well as electrosurgically.

Education

Two residents - one PGY2 and one PGY4 - rotate on the oncology service, along with third-year HMS students and fourth-year sub-interns in gynecologic oncology. The division sponsors a weekly Gynecologic Oncology Tumor Board, a multidisciplinary conference attended by members of this service, as well as pathologists, radiologists, medical oncologists and radiation therapists, to discuss every patient's clinical course and treatment options. The division also sponsors a gynecologic oncology journal club and a research meeting. Residents are responsible for daily rounds, assistance at surgical procedures and presentation of patients at Tumor Board. Weekly didactic sessions supplement the resident educational experience.

During the residents' rotation on the gynecologic oncology service, they participate in the colposcopy/laser ambulatory clinics. They are taught the principles of colposcopy and the place of laser surgery in gynecology. Training of residents is provided in colposcopy, CO2 laser, electrosurgery and cervicography. This rotation provides the resident with the opportunity to become an accomplished colposcopist and laser surgeon.

Research

The division has an active clinical research program under the direction of Dr. Stephen Cannistra, a nationally recognized medical oncologist with particular expertise in ovarian cancer. A number of clinical trials are open to patient accrual. The division is also a participating institution of the Gynecologic Oncology Group.

UROGYNECOLOGY

Peter L. Rosenblatt, M.D.
Director

Mission

The mission of the division of urogynecology and reconstructive pelvic surgery is to provide comprehensive evaluation and management of disorders of the female genitourinary tract, including urinary incontinence and pelvic organ prolapse. By offering a variety of treatment options for any specific condition, the division empowers women with the ability to actively participate in the decision-making aspect of their care. The division also provides clinical teaching in the field of urogynecology to medical students, residents and clinical fellows.

Clinical Care

The division of urogynecology was established in 1995 by Dr. Peter Rosenblatt, and has grown over the past few years to become the largest urogynecology and reconstructive pelvic surgery center in Massachusetts.

The division is well-established throughout New England as a referral center for complicated urogynecologic disorders. Patients are referred for basic and complex evaluation of incontinence and pelvic organ prolapse, as well as for conservative and surgical management of these and other benign gynecologic conditions. The clinical office staff provides a wide variety of services including complex multichannel urodynamic testing, biofeedback, peripheral afferent electrical nerve stimulation (and other forms of pelvic floor rehabilitation), behavioral modification and patient education. Physical therapists trained specifically in pelvic floor rehabilitation are available within the offices to provide conservative treatment of incontinence, pelvic pain and other related conditions. Periurethral bulking agents are also used in the office for the treatment of stress incontinence, as an alternative to more invasive surgery.

The staff of the division maintains a busy surgical practice, with inpatient and outpatient procedures currently being performed at five area hospitals. With an emphasis on minimally-invasive surgical procedures, the staff offers vaginal, abdominal and laparoscopic surgical procedures. A particular emphasis has been placed on developing innovative laparoscopic techniques, in order to perform procedures in a minimally-invasive fashion that were previously only able to be

performed via laparotomy. In terms of urogynecologic surgery, the staff currently performs laparoscopic Burch bladder neck suspension, paravaginal cystocele repair, uterosacral ligament suspension, sacrocolpopexy and sacrocervicopexy, which is becoming a popular alternative to hysterectomy for uterine prolapse. In addition, laparoscopic supracervical hysterectomy and laparoscopic myomectomy are being performed on a regular basis. The staff has also been performing sacral nerve stimulation for refractory urge incontinence for the past five years.

Over the past five years, over 1,000 tension-free vaginal slings have been performed by physicians within the division of urogynecology. This minimally-invasive, extremely effective and durable procedure has grown in popularity and has become a gold-standard in the treatment of female stress urinary incontinence. In addition, the physicians offer traditional autologous fascial slings for this condition.

Research

The division of urogynecology has been active in clinical research for the past six years. Prospective trials have included the use of peripheral afferent nerve stimulation for urge incontinence, endopelvic fascial shrinkage using radio-frequency bipolar energy for stress incontinence, and a randomized trial comparing laparoscopic Burch to the tension-free vaginal tape (TVT) suburethral sling.

Teaching

All the members of the division are actively involved in clinical teaching. Students from HMS participate both in the office setting, as well as in the operating room. Third-year residents in OB/GYN from BIDMC each spend a 10-week rotation with the physicians of the division, with an emphasis on learning minimally-invasive laparoscopic techniques.

Fellowship

The fellowship program in urogynecology at Mt. Auburn Hospital is a three-year, fully-accredited, clinical and research program, which began in 1999 and has graduated two physicians who have both gone on to academic programs on the East coast. The program consists of exposure to office evaluation and conservative management options, extensive urogynecologic surgical volume and performing clinical research in the field. The emphasis of the third year of the program is to complete original research and further develop teaching skills.

MATERNAL-FETAL MEDICINE

Benjamin Sachs, M.D.
Division Director

Mission

The mission of the division of maternal-fetal medicine is to continually provide excellent obstetrical care to all patients, to function as a resource for community and medical center-based general obstetricians, to improve understanding of obstetrical conditions and treatments, and to train physicians to provide the highest caliber obstetrical care.

Accomplishments and Goals for Academic Year 2004-2005

The division is dedicated to providing quality obstetrical care to women with vastly different complications that directly affect pregnancy. The division of maternal-fetal medicine provides high-risk obstetrical care to patients who have been referred from all over New England. The number of deliveries for the division has continued to increase over the past year. Patients are followed throughout their pregnancy by their own maternal-fetal medicine specialist, and in many cases are also delivered by them. This ensures the highest quality of care, as well as continuity of care. These are especially important to patients who may have serious medical or fetal complications.

This year the transfer program continued to expand. Many community hospitals in the metro Boston region, as well as parts of southern New Hampshire, Nantucket Island, and even Bermuda send patients to the maternal-fetal medicine service for the highly specialized and quality care that is given.

Under the direction of Dr. Benjamin Sachs, each of our perinatologists has specialized in an area of interest, allowing the program to flourish: Dr. Bruce Cohen with multiple gestations and the outreach programs; Dr. Ian Grable with the Joslin Diabetes Program; Dr. Tamara Takoudas with resident education and quality improvement; Dr. Jeffrey Johnson with maternal medical complications, including prematurity and fetal therapy; and Dr. Kee-Hak Lim with hypertensive disorders in pregnancy and the first and second trimester genetics program.

The perinatologists continue to provide ultrasounds, prenatal care and consultative services at BIDMC and the affiliated off-site practices. The division offers diagnostic and consultative services at seven community hospitals. Our satellite programs are located in Beverly, Brockton, Cambridge, Concord, Framingham, Nantucket Island, Reading, and Winchester. We also provide services at one of the Boston freestanding neighborhood health centers.

We also continue our collaboration with the Advanced Fetal Care Center at Children's Hospital of Boston. We collaborate with the pediatric surgeons, to expand the options for the treatment of fetal abnormalities, complications of identical twin pregnancies, and a multitude of other high-risk fetal anomalies.

Diabetes and Pregnancy Program

Women with diabetes, including those who develop diabetes during pregnancy, require special attention. Diabetes care is critical, both before and after conception, to ensure the health of both mother and child.

The Diabetes and Pregnancy Program, a service of Joslin Clinic and BIDMC, offers specialized, state-of-the-art diabetes care designed to meet patient's individual needs. The program is a collaborative effort of Joslin Clinic's skilled medical staff and the high-risk maternal-fetal medicine specialists at BIDMC.

Through the program, patients receive care from a multidisciplinary team of providers at one convenient location. Specialists in diabetes, including physicians, nurse practitioners, nurse educators, nutritionists and others, provide treatment. Maternal-fetal specialists provide obstetrical care, combining the latest medical expertise and technology with personalized care to meet patient's unique needs.

Education

The division continues to focus on education for the patients, physicians and residents. We have regular patient and provider satisfaction surveys done. Our results consistently emphasize that our commitment to quality of care is outstanding. Mary Rooney-Belmonte, R.N., and Michelle Christman, R.N., provide patient contact and education throughout pregnancy. They also provide updates to referring physicians regarding the status of their patients during their stay at BIDMC. Mary Rooney-Belmonte, R.N., is also involved in education for nursing and physicians at several of the off-site practices.

The division provides clinical and administrative support for the labor and delivery unit and the antepartum fetal testing service. It also offers an intensive educational milieu for residents, medical students and attending staff. There is a close relationship between the maternal-fetal medicine division and many other service and research units in the medical center, at the medical school, and the Harvard School of Public Health. Frequent clinical interchanges occur with anesthesiology, neonatology, genetics, radiology, renal medicine, endocrinology and hematology. A second-year resident and the obstetrical chief resident work in concert with the perinatal team in all academic and patient care matters.

Division members work collaboratively to provide education conferences, as well as a "hands-on" clinical experience. The focus of this education is to provide an opportunity for community practitioners to foster their skills in caring for medically compromised patients, including the sharing of practice guidelines. This program incorporates the latest evidence-based research into clinical practice.

Research

Dr. Kee-Hak Lim has a groundbreaking research project investigating preeclampsia and potential diagnostic and curative therapy for affected patients. It is being supported through a grant from Johnson & Johnson pharmaceuticals. He is also a co-investigator on a NIH-funded project investigating the role of trophoblasts and angiogenic molecules in development of preeclampsia. In addition, he is working on applying Diffuse Reflectance Spectroscopy in isolating fetal cells from maternal circulation. This work is done in collaboration with Dr. Lev Perelman and is funded by NIH.

Dr. Jeffrey Johnson has a multicenter project involving prediction of prematurity and therapy with progesterone supplementation, which is supported by a grant from the March of Dimes.

Dr. Ian Grable, as director of the Joslin Diabetes and Pregnancy Program, is involved in research and education in this field.

Dr. Tamara Takoudes performed a study that was a retrospective, observational cohort evaluating wound complications in 185 patients with type 1 and 2 diabetes, who underwent cesarean delivery in comparison to 174 non-diabetic controls. The outcome of this study showed a 2.5-fold increased risk of wound infection and separation despite similar surgical techniques and antibiotic use. The study calls for more research in possible interventions to decrease the high wound complication rate in diabetic patients undergoing cesarean delivery. Her article, "Risk of Cesarean Wound Complications in Diabetic Gestations" appeared in the American Journal of Obstetrics and Gynecology (2004;191:958-63).

All members of the MFM division are collaborating with Dr. Deborah Levine in radiology on a NIH-funded study evaluating the role of fetal MRI in diagnosing fetal intracranial abnormalities.

CLINICAL GENETICS

Virginia Kimonis, M.D.
Director

Kee-Hak Lim, M.D.
Associate Director

Mission
The clinical genetics program provides high-quality, compassionate genetic counseling for families with concerns about hereditary conditions.

Clinical Care
The goal of genetic counseling is to provide accurate information, which enables individuals, and families to make their own fully informed decisions. Genetic counseling and evaluation is offered for patients concerned about a hereditary condition in their family or a child with a birth defect or mental retardation. We offer counseling for pregnancy for women age 35 or over at delivery, and for women with family histories of genetic or rare conditions.

Program staff meets one-on-one with families to discuss their concerns, provide risk assessments and aid in choosing further testing and decision-making. For couples that desire further testing, the staff follows up with the family to discuss the results. In the event of abnormal results, ongoing supportive counseling is provided. Additionally, clinical genetics works closely with the social work department and the referring provider for families who may need additional care.

Test Results
BIDMC offers prenatal diagnostic services including chorionic villus sampling, amniocentesis, cytogenetic, biochemical and molecular genetic analysis, and fetal blood testing. The department works closely with the Cytogenetics Laboratory at BIDMC to assure that results of chromosome analysis are accurately conveyed to both patients and providers. At the medical center, staff members meet with families who deliver a baby with a possible genetic disorder or birth defect, to coordinate their infant's care with genetics consultants at Children's Hospital so that the families experience a smooth transition from one service to the other.

Education
Monthly interdisciplinary rounds are held for genetics, perinatology, OB/GYN, neonatology, radiology, cytogenetics, and social work to discuss patients continuing pregnancies with expected anomalies.

OB/GYN ULTRASOUND

Deborah Levine, M.D.

Mission
The mission of the OB/GYN ultrasound program is to deliver state-of-the-art prenatal diagnosis, utilizing the latest advances in technology.

Clinical Services
The radiology department at BIDMC has six rooms in our outpatient clinical center devoted to OB/GYN ultrasound, with Phillips 5000 and IU22 machines, allowing for top of the line imaging with 2D and 3D probes and real-time capability. We also offer OB/GYN ultrasound services at centers in the community and for inpatients. Our volume is approximately 16,000 OB/GYN examinations on-site per year. We train residents and fellows in the radiology and OB/GYN departments.

In addition to imaging, procedures performed include hysterosalpingography, sonohysterography, amniocentesis, pelvic drainages and guidance for chorionic villous sampling. We also offer obstetric magnetic resonance imaging for cases where sonographic examination is inconclusive.

Research
Clinical research interests of our faculty include studies on education in ultrasound, use of Doppler in OB/GYN imaging, and use of PACS in remote diagnosis for OB/GYN cases. Obstetric magnetic resonance imaging projects include use of MR in diagnosing pregnant patients with right lower quadrant pain and accuracy of MR (and impact on patient care) in cases of complex fetal anomalies. An NIH grant ($450-500,000 direct costs per year for 5 years) funds a study of fetal ventriculomegaly and correlation of prenatal ultrasound and MR indices with postnatal outcomes.

NEONATOLOGY

DeWayne Pursley, M.D., M.P.H.
Neonatologist-in-Chief

Mission

The department of neonatology is committed to providing personalized, high-quality care to newborn patients and their families. The department is also committed to maintaining a stimulating, supportive environment for teaching and research that conveys and enhances knowledge of newborn health and care.

Clinical Care

The Neonatal Intensive Care Unit (NICU) program provides care to over 1,500 newborns each year. More than 800 of these newborns require admission to the unit, while the remainder are evaluated and triaged to the newborn nursery. The NICU average daily census is now 40.

The multidisciplinary NICU team provides comprehensive, family-oriented care. The team, which includes nurses, physicians, neonatal respiratory therapists, social workers, neonatal dieticians, an occupational therapist and a pharmacist, is extensively trained in the care of the high-risk newborn and provides a full range of services for neonatal patients and support for their families. Through a tightly integrated consultation system with the maternal-fetal medicine staff, genetic counselors and Children's Hospital pediatric sub-specialists, the NICU team monitors all maternal admissions likely to result in the delivery of a newborn requiring intensive care, and then provides necessary care in a coordinated multidisciplinary model.

The NICU continues to provide cutting-edge therapy through new technologies, including inhaled nitric oxide for pulmonary hypertension. It also makes potentially groundbreaking clinical research protocols available to eligible patients.

Newborns resulting from community hospital maternal-fetal transfer and delivery continue to represent a significant number of the patients in the NICU. The NICU is able to retro-transfer the great majority of these patients back to their community hospitals when clinically ready. Additionally, many of the newborns whose mothers' care originated at BIDMC are also transferred to their local community hospitals.

Neonatal nurse practitioners, working under the clinical supervision of department faculty, remain active in the care of high-risk newborns at BIDMC. Together with attending neonatologists, they provide around-the-clock coverage in the NICU and participate in the teaching of nurse practitioner students, as well as HMS students.

Neonatal-perinatal fellows continue to serve an important clinical role in the NICU. During monthly rotations, they continue to bring new knowledge and clinical innovations, which support the unit's goal to provide care at the leading edge.

Newborn Nursery

The Cochran Newborn Service provides comprehensive newborn care to those infants whose primary pediatric providers are not members of the BIDMC staff. This service has grown substantially over recent years and in 2003 provided care to over 2,000 newborns.

All nursery babies undergo hearing screening under a program that was among the first universal newborn screening programs developed in the Commonwealth and has been lauded by the Massachusetts Department of Public Health. Car seat position testing is also provided to all premature infants prior to discharge.

Education

BIDMC continues to be one of the four clinical training sites for the ACGME-approved Children's Hospital neonatal-perinatal medicine training program. This program provides fellows with a strong clinical base, as well as research training. Fellows in this program rotate monthly through BIDMC, providing care to newborns and their families and honing their team leadership and patient management skills in the NICU and high-risk antepartum consult service. Eight of the current 18 fellows are also receiving research mentoring from BIDMC neonatology faculty.

Each year, the department of neonatology offers an AAP-approved training course in neonatal resuscitation to all obstetrical and anesthesia residents. First-year residents receive their initial training, while all other residents are offered annual refresher courses. The department also offers formal clinical training through HMS for HMS-III students on a five-day rotation through the newborn nursery, and HMS-IV students on a month-long elective subinternship in the NICU.

Departmental goals include the further development of innovative technology for education; intensive, direct mentoring of active learners throughout the process of providing newborn care; ongoing monitoring of student satisfaction in meeting learning objectives; and the seamless integration of teaching into policies, practices, and routines of newborn care.

Research

The mission of the department of neonatology research program is to advance neonatal health and health care through excellence and innovation across the spectrum of clinical research. Research activities of department faculty span the spectrum of clinical research and include outcomes research, clinical informatics, decision analysis, decision support, econometric analysis, clinical epidemiology, clinical trials, long-term follow up, health policy analysis, organizational behavior and program evaluation.

In recent months, funding has been utilized to refine the infrastructure of the research program. New positions to support administration, study coordination, biostatistical support and data management have recently been filled.

Current efforts are focused on identifying new research opportunities, fostering further collaborations with other departments and institutions, and developing or refining programs in neonatal clinical research training.

REPRODUCTIVE ENDOCRINOLOGY REPRODUCTIVE ENDOCRINOLOGY AND INFERTILITY

Richard H. Reindollar, M.D.
Division Director

Mission

The mission of the division of reproductive endocrinology and infertility is to provide a broad spectrum of investigative and therapeutic modalities for the full range of reproductive and endocrine disorders. The division provides cutting-edge research and education for future physicians and the community.

Clinical Care

The division's clinical care services include a highly successful in vitro fertilization program (Boston IVF), andrology and gynecologic endocrinology laboratories for neuroendocrine and dynamic endocrine testing, assessment of sperm and ovum fertilization potential, as well as micro-surgical operating facilities. Established in 1986, Boston IVF has earned an impeccable reputation in the national and regional medical communities as one of the first and most successful advanced fertility treatment facilities in the United States. Boston IVF is the largest assisted reproductive technology center in the United States. An unmatched commitment to scientific and clinical research has resulted in a number of significant "firsts" in New England, including the first deliveries for GIFT, embryo cryopreservation, donor oocyte, and the first baby born from ICSI. Boston IVF developed quality standards and objectives to not just improve what they do, but to set the bar for quality care in reproductive medicine. As a result of this work, Boston IVF earned the unique distinction of becoming the first fertility provider in North America to become certified to ISO 9001:2000 standards.

Boston IVF is a full-service clinical and academic reproductive endocrinology center that includes as its primary focus the largest ART (assisted reproductive technology) program in the US. Its clinical services include medical and surgical management of couples with reproductive failure, identification and management of menstrual abnormalities and their lifelong associated health hazards, management of menopause, the surgical repair of congenital reproductive anomalies, and care of young girls and women with pubertal abnormalities. The Boston center is located four blocks from the main BIDMC campus; additional centers are located in Cambridge, Framingham, Quincy and Waltham. Patients are also seen in offices in New Hampshire, Maine and on Nantucket Island. Patients can meet with their Boston IVF physician and perform necessary diagnostic and monitoring at any of these locations. In addition, Boston IVF brought the first infertility care by a reproductive endocrinologist to Bermuda. Patients are seen in Bermuda several times a year and come to Boston IVF for ART.

Over 50,000 patient visits per year occur at Boston IVF, including approximately 500 reproductive surgeries, over 2,000 IVF and 5,000 non-IVF ART cycles each year. More than 10,000 babies have been born as a consequence of ART procedures performed at Boston IVF. Surgeries include diagnostic and operative endoscopy (laparoscopy/hysteroscopy) for developmental and acquired reproductive tract abnormalities in both men and women, laparotomy for developmental uterine anomalies, uterine fibroids, and severe endometriosis that cannot be treated by endoscopic surgery, corrective surgery to treat vaginal agenesis and other reproductive tract anomalies, and endometrial ablative surgeries for abnormal uterine bleeding. The full-service ART program incorporates state-of-the-art methods, including IVF, ICSI, assisted hatching and a donor oocyte program.

Education

The division of reproductive endocrinology and infertility (REI) provides a well-rounded program of teaching and clinical activities to enable students, residents and fellows to become well versed in the basic scientific aspects of the field, as a foundation upon which to build a strong understanding and competency in clinical evaluation and management of relevant problems. The division is actively involved in the HMS student teaching and tutorials. Dr. Richard Reindollar is the co-planner of the HMS pathophysiology course Human Systems Module II, Endocrinology of Growth, Metabolism, and Reproduction. Many members of the division actively participate in the course with lectures and tutorials. Weekly clinics for gynecologic endocrinology patients provide an opportunity for clinical care and teaching. Residents and fellows are involved in the in-hospital medical management and surgical care of the patients admitted under the aegis of the division. Patients with menstrual abnormalities are referred to a monthly

endocrine clinic at the BIDMC main campus that the REI fellows and OB/GYN residents are involved in. Teaching in the clinical setting is supplemented by a formal patient review conference following the weekly clinic session, monthly grand rounds presentations, periodic didactic talks and a weekly conference, as well as bedside and operating room teaching on an ongoing basis.

The fellowship training program is a three-year program designed to provide the fellow with a protected basic research experience and a well-rounded clinical experience, with exposure to all aspects of reproductive endocrinology and a very high-volume ART program. The first 18 months are devoted primarily to basic science research, with the divisional investigations in the areas of molecular aspects of reproduction. Numerous other possibilities exist within the Harvard system for this basic research. During this time, one session a week is spent in a well-rounded REI clinical setting. The last 18 months are primarily devoted to the clinical experience, with an additional research time allotment. All aspects of reproductive endocrinology are represented including pediatric, adolescent, medical endocrinology, contraception, and male and female infertility. During the last six months, 30% of time is available for outcomes-oriented research or to return to the basic laboratory. The fellow spends one weekend monthly performing numerous ART procedures during all three years. Weekly conferences include: RE case conference, lecture series (outside and institutional lectures), IVF/Research, grand rounds and monthly journal clubs.

Research

The molecular genetics laboratory, under the direction of Dr. Anny Usheva, includes state-of-the-art facilities for identification of genes and analyzing gene expression. The molecular biochemistry laboratories are fully equipped for experiments in reproductive physiology, endocrinology and membrane biochemistry. The molecular laboratory has centered much of its work around the study of women with congenital absence of the uterus and vagina, to identify genes involved in müllerian development. More recently it has initiated a large study to investigate the processes involved in ovarian aging in mice and humans.

Dr. Richard H. Reindollar, director of the division of reproductive endocrinology and infertility, has been awarded grants by the National Institute of Health (NIH) for the two largest infertility studies funded at a single site. The FASTT Trial, Conventional Infertility Therapy vs. Fast Track to IVF, now in its last year of randomization, is studying two different infertility treatment paradigms for couples with the female partner under 40 years of age. The FORTT Trial, Optimal Infertility Therapy RCT: Women 40 and Older, recruitment presently underway, is analyzing treatment paradigms for couples with the female partner ages 40-43 years of age. These studies are being performed with members of the Harvard School of Public Health. Boston IVF has a large database and high patient volume, which provides an ideal resource for both federally-funded and non-funded clinical studies.

STATISTICS

Obstetrical Service – June 30, 2003 to July 1, 2004

Outpatients New (resident clinic)	**135**
Total Deliveries	**5133**
Cesarean Deliveries - Total	**1768**
Cesarean Deliveries - Primary	**1137**
Cesarean Delivery Rate - With Maternal -Fetal Medicine	**34%**
Vaginal Birth After Cesarean Delivery	**95**
Breech Delivered Vaginally	**6**
Forceps Deliveries	**34**
Vacuum (extraction) Deliveries	**180**
Multifetal Delivered Vaginally	**35**
Pregnant Diabetics (admitted / discharged) Type I, II, and Gestational	**323**
Preeclampsia, Gestational Hypertension & Chronic Hypertension Patients (admitted / discharged)	**312**
Multiple Gestations	**202**
Low Birth Weight Infants (500 - 2500 grams)	**517**
Surgical Procedures on Antenatal Patients (excluding ectopic pregnancies)	**110**
Cardiac Disease in Pregnancy	**12**

Gynecology Service – June 30, 2003 to July 1, 2004

Outpatient - New visits (resident clinic)	511
Dilation and curettage	847
Cervical cone biopsy	10
Cervical Laser/LEEP/LOOP	136
Colporraphy/AP repair	36
Hysterectomy - Total, all types	**486**
Radical	5
Abdominal /or lap assisted abdominal	358
Laparoscopically assisted vaginal hysterectomy	23
Vaginal with repair or TVT/cysto	64
Vaginal without repair	36
Hysteroscopy - Total , all types	**419**
Hysteroscopy	365
Hysteroscopy with ablation	54
Laparoscopy-diagnostic and operative	268
Mini-Laparotomy	68
Myomectomy	86
Ovarian cystectomy	33
Resection pelvic mass	55
Trans-vaginal Tape, with or without AP repair	77
Tubal ligations—Total, all types	**107**
Laparoscopic	81
Postpartum	26
Vulvar or vaginal laser therapy	11
Vulvectomy-partial or radical	17
Outpatients Total Visits	**3909**

NURSING

Patricia McNamee, R.N.
Labor and Delivery

Deirdre Burke, R.N.
Postpartum

Phyllis West, R.N.
Gynecology

Mission

OB/GYN nursing is committed to caring for women for the full continuum of their lifecycle health care needs. We are committed to continuity of care by the practice of primary nursing.

Clinical Care

The obstetrical division of nursing is composed of labor and delivery, high-risk antenatal, postpartum and newborn nursery. Special services include the neonatal intensive care unit (NICU), lactation support services and the ambulatory testing unit. Additional support for patients is provided through the Learning Center, childbirth education and the baby carriage. The gynecologic nursing division provides full inpatient care, including management of complex gynecologic surgical and oncology patients.

We are proud to have inherited the rich legacies of professional nursing that were associated with both the Beth Israel and Deaconess Hospitals before our merger in 1996. Since then, we have continued to establish exemplary, integrated programs of service and support that will help to ensure continued excellence in nursing practice into the millennium.

OB/GYN QUALITY IMPROVEMENT / ASSURANCE

Mission

The mission of the OB/GYN quality improvement/assurance program at BIDMC is to monitor care delivered to the obstetric and gynecologic patient population.

Patient Safety

Patient safety is one of the greatest challenges facing our health care system. According to the Institute of Medicine Report (published in 2000), between 44,000 and 98,000 deaths occur in hospitals in the United States every year due to adverse events. It is our moral obligation to improve the safety of childbirth and in the process we can reassure the public and our legislatures. This gives us a stronger argument for tort reform. In 2002, funded by the Department of Defense and Harvard's Risk Management Foundation, we adapted the principles of Crew Resource Management (team training). The concept of Crew Resource Management (CRM) originated in the airline industry and all three branches of the military service. The implementation of these methods in the BIDMC labor and delivery unit was a first in the practice of obstetrics, and one of the first times ever in medicine. We have just completed a 15-hospital randomized control trial with the objective of proving that this approach can improve patient safety. Since the introduction of CRM at BIDMC, we have noted a dramatic improvement in patient safety, while simultaneously noting a dramatic rise in patient and staff satisfaction. We believe that team training is effective, especially when built on a solid base of quality assurance and quality improvement programs. The evaluation and adoption of team training has dramatically affected the culture of safety in our department of obstetrics. As a result of our leadership role in this field, we have begun to see the concepts of team training applied to other areas of health care, including emergency departments, operating rooms and intensive care units.

Quality Assurance Committee

The Quality Assurance Committee cases are selected for review based on indicators defined by JCAHO, ACOG and Harvard Risk Management Foundation. Information is gathered from the admitting department's list of discharge codes, OR reports and the OB database. All staff members in the OB/GYN department are encouraged to submit provider-raised issues to the OB/GYN quality assurance department if they have a specific concern regarding a patient's care.

The OB/GYN Quality Assurance Committee consists of staff representing all divisions and call groups within the department of OB/GYN. Members of the committee serve for a minimum of two years and render the commitment needed to achieve the goals of monitoring and enhancing quality patient care. All the chief residents sit on this committee.

Quality Improvement Committee

The focus of continuous quality improvement is on improving the processes of care, rather than on identifying individual deficiencies. Continuous quality improvement requires ongoing monitoring and evaluation of clinical patient care. Priorities are given to the aspects of care that are high volume, high-risk and problem prone.

The committee identifies problems based on data analysis, referrals from the Quality Assurance Committee and provider-raised issues. Focus areas include processes of care, variation and causes of variation, and prevention of adverse outcomes or near misses. Once a problem is identified, data is obtained to verify the problem. An action plan is then formulated and disseminated to the appropriate personnel. All the chief residents sit on this committee.

SOCIAL WORK

Barbara Sarnoff Lee, M.S.W.
Director

Mission

The OB/GYN social work division provides direct OB/GYN clinical care, consultation and education to patients, families and staff at BIDMC. The staff has expertise in women's health issues across the developmental lifecycle. They also have specialized knowledge as it pertains to high-risk pregnancies, HIV-AIDS in women, perinatal bereavement, pregnancy termination, gynecological cancers, child welfare issues, substance abuse, domestic violence, and menopause. In addition to the direct clinical care and counseling with patients and families, the social work department sponsors several specialty programs, through the Center for Violence Prevention and Recovery, to address the health risks associated with violence.

The Center for Violence Prevention and Recovery encompasses Safe Transitions, a domestic violence intervention program, and the Rape Crisis Intervention Program.

Safe Transitions — Domestic Violence Intervention Program

Crisis intervention — Advocacy and counseling for patients and staff who are in coercive, controlling or abusive relationships

Consultation—Staff are on call 24 hours, 7 days a week to provide guidance and resource information to other members of the staff and their patients

Safe Bed — Safe Transitions is one of the first and only Boston-based programs to provide anonymous, free overnight shelter for patients for whom it would be unsafe to return home and who have no safe alternatives

Support Groups — These groups provide a forum for patients and staff to share their stories and strategies for survival. Outreach efforts have been made to particular area colleges and universities to initiate an education/support group for graduate and undergraduate students

Rape Crisis Intervention Program

- Emergency department, medical and psychological services for sexual assault patients. Trained rape crisis counselors provide crisis counseling for rape trauma patients
- Follow-up crisis counseling for sexual assault patients and their family and friends, which focuses on the emotional impact of the trauma
- Follow-up medical care through OB/GYN services
- In-service training for multidisciplinary hospital staff in treating rape trauma
- Clinical research on treatment and recovery from sexual assault

COMMUNITY MEDICINE

Martin November, M.D., M.B.A.
Director

The community medicine service provides obstetric and gynecologic care to a culturally and ethnically diverse population of urban and suburban women. All inpatient obstetric care, including labor and delivery, and inpatient gynecology, takes place at BIDMC in Boston. In keeping with the concept of primary care, a primary obstetrician / gynecologist coordinates care for all women at her site. Each physician works with the support staff at the neighborhood health center to ensure the patient's transition in and out of the hospital is seamless.

Neighborhood Health Centers and Their Principal Communities

Bowdoin Street Community Health Center — Cape Verdian, Hispanic, Asian, African American

Dimock Community Health Center — African American, Hispanic

Fenway Community Health Center — Gay and Lesbian

Roxbury Comprehensive Community Health Center — African American, Hispanic

South Cove Community Health Center — Asian

THE PARENT CONNECTION

Christine Sweeney, L.I.C.S.W.
Program Director

Welcoming a new baby into the home can be both an exciting and overwhelming experience, especially for first-time parents. At BIDMC, our patients represent a very diverse group of parents. However, for most adjusting to parenthood is a major transition in the life of any individual and couple. The Parent Connection, the only hospital-based program of its kind in Boston, provides families with continued support after they leave the hospital through three distinct areas of service: the mentoring moms program, support groups and a monthly lecture series.

The goal of the Parent Connection is to enhance parenting skills by providing new families support in their adjustment to parenthood, to link families into both medical center and community-based resources, and to encourage a long lasting relationship to BIDMC. By intertwining the services of volunteers, hospital staff and community services, the Parent Connection helps families begin parenting on a positive note.

INTERNATIONAL HEALTH CARE

Benjamin Sachs, M.D.
Director

The department has developed and raised funds for women's and children's health centers in a number of developing countries. These clinical programs have been used as laboratories for developing new approaches to primary health care for women and children. In addition they provide educational experiences for our residents and faculty interested in international health. In addition, many members of the department have provided consultation in other parts of the world.

The funding has been provided through multiple sources, including USAID and philanthropy. The centers in the Philippines and Armenia, once established and up and running for a few years, were turned over to the local authorities. Transfer of authority was successfully achieved in each case.

Philippines (1987) — High-risk obstetrics center, Children's Hospital, Quezon City

Armenia, Yerevan (1992 - 1996) — Primary care program for women - 82,000 patient visits

Ukraine, Dniepropetrovsk (1999 - present) — Primary care program for women and children, Dniepropetrovsk - 20,000 patient visits per year

RESEARCH

The department of obstetrics and gynecology at BIDMC has been fortunate to be awarded over 8.5 million dollars, in federal and non-federal grants, for 2004 and beyond. The department is comprised of five divisions: general obstetrics and gynecology (including community health), genetics, reproductive endocrinology and infertility, gynecological oncology, gynecological urology and maternal-fetal medicine. Approximately 5,000 deliveries are performed at BIDMC each year. Our reproductive endocrinology group also operates the largest in vitro fertilization program in the United States, performing over 3,000 cycles of IVF annually. The departmental mission dictates that we provide healthcare to all, demonstrate excellence in teaching for medical students and residents, and foster outstanding clinical and bench research. Through close collaboration with other departments at the medical center and within HMS, the department has recently expanded its basic research program. Through such collaborative efforts, significant advances have been made in our understanding of the pathogenesis of preeclampsia and cystic fibrosis. Potential new therapies are being explored in both areas. The department also places special emphasis on epidemiology and public health policy as it relates to women's health both in the United States and abroad. The department is leading a national effort to assess ways in which team training might significantly improve patient safety.

PUBLIC HEALTH AND EPIDEMIOLOGY RESEARCH

Benjamin Sachs, M.D.
Harold H. Rosenfield Professor, Harvard Medical School; Professor, Harvard School of Public Health; Chief, Department of Obstetrics and Gynecology

Patient Safety / Health Care Quality Research

Dr. Sachs is the principal investigator on a national randomized control trial (funded by the Department of Defense) including 15 hospitals to evaluate the role of team training to significantly reduce medical errors in obstetrics. The goal of this project is to demonstrate a 40% reduction in medical errors, as well as improvement in patient and staff satisfaction. The project has been assisted by many national organizations including the American College of Obstetrics and Gynecology.

International Health Care

The department has developed and raised funds for women and children's health centers in a number of developing countries. These clinical programs have been used as laboratories for developing new approaches to primary health care for women and children. In addition they provide educational experiences for our residents and faculty interested in international health.

The funding has been provided through multiple sources, including USAID and philanthropy. Each of the clinics listed below were run through our project for a finite period of time, after which operation of the clinic was turned over to the local authorities. Transfer of authority was successfully achieved in each case.

Philippines (1987) — High-risk obstetrics center, Children's Hospital, Quezon City

Armenia, Yerevan (1992 – 1996) — Primary care program for women — 82,000 patient visits

Ukraine, Dniepropetrovsk (1999 – present) — Primary care program for women and children, Dniepropetrovsk — 20,000 patient visits per year

By virtue of my sitting on the Board of Harvard Medical International, the department participates in HMI's outreach to improve healthcare and education worldwide.

Related Publications

Sachs BP. — Vaginal birth after cesarean: a health policy perspective. *Clin Obstet Gynecol. 2001 Sep;44(3):553-60*

Sachs BP, Kobelin C, Castro MA, Frigoletto F. — The risks of lowering the cesarean-delivery rate. *N Engl J Med. 1999 Jan 7;340(1):54-7*

Fretts RC, Rodman G, Gomez-Carrion Y, Goldberg R, Sachs BP, Myers E, Kessel B. — Preventive health services received by minority women aged 45-64 and the goals of healthy people 2000. *Womens Health Issues. 2000 Nov-Dec;10(6):305-11*

Sachs BP, Fretts RC, Gardner R, Hellerstein S, Wampler NS, Wise PH. — The impact of extreme prematurity and congenital anomalies on the interpretation of international comparisons of infant mortality. *Obstet Gynecol. 1995 Jun;85(6):941-6*

Ricciotti HA, Chen KT, Sachs BP. — The role of obstetrical medical technology in preventing low birth weight. *Future Child. 1995 Spring;5(1):71-86*

Sachs BP, Korf B. The Human Genome Project: implications for the practicing obstetrician. *Obstet Gynecol. 1993 Mar;81(3):458-62*

Sachs BP, Hellerstein S, Freeman R, Frigoletto F, Hauth JC. — Home monitoring of uterine activity. Does it prevent prematurity? *N Engl J Med. 1991 Nov 7;325(19):1374-7*

Sachs BP, Penzias AS, Brown DA, Driscoll SG, Jewett JF.—Cancer-related maternal mortality in Massachusetts, 1954-1985. *Gynecol Oncol. 1990 Mar;36(3):395-400*

Sachs BP, Oriol NE, Ostheimer GW, Weiss JB, Driscoll S, Acker D, Brown DA, Jewett JF. — Anesthetic-related maternal mortality, 1954 to 1985.

Sachs BP, Brown DA, Driscoll SG, Schulman E, Acker D, Ransil BJ, Jewett JF.—Hemorrhage, infection, toxemia, and cardiac disease, 1954-85: causes for their declining role in maternal mortality. *Am J Public Health. 1988 Jun;78(6):671-5*

MEDICAL EDUCATION RESEARCH WOMEN'S HEALTH

Hope Ricciotti, M.D.
Assistant Professor of Obstetrics, Gynecology and Reproductive Biology, Harvard Medical School; Chair, OB/GYN Clerkship Committee, Harvard Medical School; Deputy Director for Education, Harvard Center of Excellence in Women's Health; Harvard Medical School Women's Health Theme Director; Chair, Professional Education Working Group of the National Center of Excellence in Women's Health Education; Clerkship Director, OB/GYN Core Clerkship at BIDMC

Dr. Ricciotti received her undergraduate degree from Brown University and medical degree from Dartmouth Medical School. After completing her residency at BIDMC, where she served as chief resident, Dr. Ricciotti joined the faculty of the department of obstetrics and gynecology. She is currently an assistant professor of obstetrics, gynecology, and reproductive biology at HMS.

Dr. Ricciotti is the clerkship director for the OB/GYN core clerkship at BIDMC and HMS and the chair of the Harvard Medical School OB/GYN Clerkship Committee. She is the deputy director for education at the Harvard Center of Excellence in Women's Health and the HMS Women's Health Theme director, roles in which she oversees the incorporation of women's health into the curriculum at Harvard Medical School. She is also the chair of the Professional Education Working Group of the National Center of Excellence in Women's Health Education.

In addition to education of the medical community and improving patient care, Dr. Ricciotti is committed to education of the public. She has written for O, The Oprah Magazine, Glamour, Fit Pregnancy, Pregnancy Magazine, and Prevention Magazine. She and her chef/husband have co-authored the following: The Pregnancy Cookbook (W.W. Norton, 2002) The Menopause Cookbook (WW Norton 2000) Breast Cancer Prevention Cookbook (WW Norton 2002), and The Healthy Family Cookbook (WW Norton, 2004). She has appeared on Good Morning America, the Today Show, Lifetime Live, and the TV Food Network. She is a member of Lluminari, a health education company committed to developing informational, inspiring and motivating multi-media programs, using the latest, science-based, gender-specific knowledge.

Dr. Ricciotti's current projects include a clinical trial on a natural soy supplement for menopausal symptom reduction, a randomized trial of an Obstetrical Virtual Patient as teaching tool for medical students, and curriculum reform in women's health.

Working in collaboration with HMS and the Harvard Center of Excellence in Women's Health, the department has developed and raised funds for projects that enhance medical education in women's health. These educational projects are multidisciplinary endeavors, bringing together physicians and educators from other disciplines to improve the education of medical students and to enhance the teaching skills of residents.

The funding has been provided through multiple sources including, the US Health and Human Service Department, Pharmaceuticals, the Macy Foundation, the BIDMC department of OB/GYN, and HMS.

Current Projects

Harvard Center of Excellence in Women's Health — funded by HHS since 1999, our department provides the leadership in educational projects to enhance the teaching of medical students in women's health as well as to enhance the women's health education of internal medicine residents.

Women's Health Theme - Harvard Medical School — funded by HMS as well as the Lily Foundation for Women's Health, our department leads to effort to better integrate women's health into the HMS curriculum.

Obstetrical Virtual Patient Project — funded by the Macy Foundation, our department authored a normal pregnancy virtual patient as part of a full series produced by the Shapiro Institute for Education and Research. The educational effect of the OB Virtual Patient as a teaching tool is currently being evaluated in a randomized, controlled study of HMS students, funded by the department of obstetrics & gynecology.

Resident as Teacher Program — our department is committed to teaching our residents to be academic teachers, and is working jointly with the HMS Resident as Teacher Program to formally enhance our resident curriculum by providing instruction on teaching skills.

Resident-Led Educational Research Projects

- "Teaching Cards" emphasizing important medical student learning objectives to enhance teaching "on-the-fly"
- Evaluation of simulated, videotaped, one-on-one teaching sessions as a tool for enhancing resident teaching

Research

The effect of a novel daidzein-rich isoflavone-aglycone extract from soy on hot flash frequency and severity in menopausal women

Hope A Ricciotti, M.D.; Lalita Khaodhiar, M.D.; Weijun Pan, M.D.; Joyce Koh, B.S.; Jinrong Zhou, Ph.D.; and George L Blackburn, M.D., Ph.D.

Isoflovones are one of the several classes of phytoestrogens, compounds that can exert both estrogenic and antiestrogenic properties. Daidzein and genistein are isoflavone that are found in rich supply of soybeans and soy products. Available data on isoflavone in treatment of menopausal symptoms has been inconclusive and the studies with positive results have reported only a slight response. This in part may be due to differences in methods used to isolate isoflavones, concentrations of bioavailable isoflavone and composition of isoflavones used.

In this randomized controlled study, we are examining the effect of a novel daidzein-rich isoflavone-aglycone extract from soy germ fermentation with Koji fungus (Aspergliius awamori) producing glycosidase efficiency on the severity and frequency of hot flashes in postmenopausal women.

OBSTETRICS AND GYNECOLOGY

Martin November, M.D., M.B.A.
Instructor of Obstetrics and Gynecology, Harvard Medical School

Major research and clinical interest focuses on health care quality, specifically as it relates to the underserved.

Current Research

- Cost effectiveness analysis of vaginal birth after cesarean (VBAC), looking at the lifetime cost effectiveness of implementing a policy of repeat cesarean section versus allowing for a trial of labor *This publication currently is being prepared for publication*
- Resident Reporting of Medical Error in OB/GYN using residents to identify both adverse and near adverse events in OB/GYN as part of their regular rounds
  Collaborators: Lucy Chie, M.D., OB/GYN and Saul Weingart, M.D., internal medicine
  This publication currently is being prepared for publication
- Co-investigator for a case-control study of obstetric malpractice claims within Harvard involving fetal distress. Part of a larger study entitled The Malpractice Insurers' Medical Error Prevention Study (MIMEPS), looking at how to improve the quality of medical care through careful analysis of medical malpractice claims. The obstetric research is a collaborative study with faculty from Brigham and Women's Hospital and the Harvard School of Public Health.
- Exploring the impact of applying systematic problem-solving methods adopted from the Toyota Motor Corporation to improve the delivery of healthcare in outpatient surgery Collaborators: Stephen Cohen, M.D., anesthesia and Dr. Steven Spear at Harvard Business School
  Grant application submitted to CRICO
- The development of an administrative compensation system for obstetric adverse events Collaborator: Dr. Troyen Brennan at Brigham and Women's Hospital

OPTICAL DETECTION OF DISEASE

Lev T. Perelman, Ph.D.
Associate Professor, Harvard Medical School; Director, Biomedical Imaging and Spectroscopy Laboratory

Lev T. Perelman is associate professor at Harvard Medical School and director of Biomedical Imaging and Spectroscopy Laboratory in the department of obstetrics and gynecology, Beth Israel Deaconess Medical Center. Prior to that he was principal scientist at MIT, where his research interest was using optical spectroscopy to diagnose disease. He conceived and developed biomedical light scattering spectroscopy (LSS) recently applied for non-invasive detection of early precancerous changes in epithelial tissues and tissue characterization on sub-cellular scale. His present research interest involves application of optics to obstetrics and gynecology, cell biology and detection of disease.

Research Projects (2001 – present)

Dynamic Monitoring of Sub-Cellular Morphology — Dynamic monitoring of sub-cellular morphology with light scattering spectroscopy; non-invasive optical karyotyping of embryos produced in in vitro fertilization; assessment of embryo morphology; monitoring of toxic effects of drugs and chemicals on embryo development
Funded by: NIH–$1,375,058, DOD–$240,322, DOD/CIMIT–$321,122 (pending)

Detection of Fetal Nucleated RBC in Maternal Blood — Development of an optical spectroscopic technique for extracting fNRBC from peripheral blood of pregnant women for non-invasive prenatal diagnosis.

Optical Detection of Alzheimer's Disease — Diagnose Alzheimer's disease by detecting presence of senile plaques and neurofibrillary tangles using diffuse reflectance and light scattering spectroscopy
Funded by: Department of Veteran Affairs–$94,000, $50,000 (pending)

Optical Detection of Preinvasive Cancer — Development of a diagnostic screening tool for rapid survey of large epithelial surfaces and reliable real-time determination of regions suspicious for dysplasia and carcinoma.
Funded by: NSF–$119,832, DOD/CIMIT–$138,964, NIH/CC–$96,200, NIH–$2,638,590 (pending)

Optical Detection of Preinvasive Cancer [1,2,7,8,9,11,14,15,16,18,22]

The purpose of this program is to provide a physician with a diagnostic screening tool, which will enable him to rapidly survey the epithelial tissue in vivo and allow him to determine with high probability and in real-time, regions of dysplasia and carcinoma. It will be able to distinguish between the categories of adenocarcenoma, high-grade dysplasia, and low-grade dysplasia, indefinite for dysplasia and non-dysplastic tissue. It will be able to perform measurements of the full length of an organ in about ten minutes and provide the information in real time. Suspicious areas can then be biopsied and the diagnosis verified. This approach is vastly superior to the present strategies of performing either systematic or random biopsies. Thus, it will provide a powerful tool for screening large population of patients for early precancerous changes.

This instrument will be based on the technique of light scattering spectroscopy (LSS), which has been demonstrated in a proof-of-principle study to be able to perform such measurements in the epithelial tissue of five different organs, including BE. The advantages of the proposed technique are that it greatly simplifies the time and labor involved in performing screening and obtaining diagnoses, will cause less patient discomfort, require fewer biopsies, and it can help the pathologist to base his diagnosis on uniform quantitative criteria, making the diagnosis more consistent. Because of these advantages, it should vastly improve the probability of detecting potential malignancies in the early stages, when cures are possible, and it should be highly cost effective. Since tissue is not necessarily removed, it makes possible progression studies. Such studies may determine accurate predicative factors for the outcome of the disease, and thus simplify the decision in the choice of treatment.

Dynamic Monitoring of Sub-Cellular Morphology [12,13,20,21,23]

The overall objective of this project is to develop and test a novel technique for non-invasive dynamic monitoring of subcellular structure, which can be used in multiple areas of biomedical research. Based on the technique, we will develop an instrument to scan biological cells with focused laser beams at multiple wavelengths and collect elastically scattered light using a confocal arrangement. Collected light, elastically scattered by various subcellular organelles and structures, will provide real time information about morphological, biochemical and physical properties of various regions of the living cell and their function. To extract this information we will combine the principals of light scattering spectroscopy (LSS) with confocal laser scanning microscopy (CLSM). LSS is an optical technique, which relates spectroscopic properties of light elastically scattered by small particles to their physical properties, such as size, refractive index and shape. CLSM is an optical technique developed to resolve biological structures within a translucent object with micron resolution. LSS has recently been applied to biological problems by this investigator and his colleagues primarily to detect early cancer. The multispectral nature of LSS enables this technique to achieve a resolving power beyond the Rayleigh limit by combining the information obtained at many different wavelengths. The new technique will be capable of determining quantitative parameters of microscopic biological structures, such as, for example, characteristics of embryo morphology and stage of development as a function of time or morphological properties related to early precancerous changes on subcellular scale.

Optical Detection of Alzheimer's Disease [17,19]

Alzheimer's disease (AD) is the most common form of dementia. It is estimated that in the United States alone, over 4 million people have AD. Prevalence is increasing with the increasing average age of the population. Yet despite recent advances in clinical diagnosis and the search for biological markers, definitive diagnosis of AD still requires neuropathological examination of brain tissue, typically post-mortem. Improved diagnosis of age-associated neurodegenerative diseases is therefore a high priority. Particularly in the current atmosphere of rapid development of pharmaceutical interventions, the need for an in vivo method to detect onset early and to monitor the development of AD are crucial. The neuropathological hallmarks of AD are senile plaques (SPs) and various forms of neurofibrillary pathology, including neurofibrillary tangles (NFTs), neuritic threads (NTs) and dystrophic neurites surrounding some SPs. Spectroscopic techniques such as near infrared (NIR) fluorescence and Raman scattering have proven useful for identifying AD brain tissue. We are developing an optical technique that will detect differences in absorption and light scattering properties of SPs, NFTs and NTs. In this technique, optical fibers positioned on the patient's scalp will deliver visible and NIR light and will collect reflected light. Since the optical properties of both the overlying skull and brain tissue are dominated by scattering and have rather small absorption, light can penetrate through the skull to probe the chemical and morphological composition of the cortex. By using both light scattering and reflectance spectroscopy we expect to be able to detect both chemical and morphological changes in Alzheimer's brain at the earliest possible stages. We have been working to identify absorption and scattering signatures of Alzheimer's brain and to detect them in order to differentiate diseased (AD) and normal control (non-AD) brains. Recently we have successfully tested our approach in situ on intact post-mortem specimens and in vivo on Alzheimer's patients.

Related Recent Publications

1. **Backman V, Wallace M, Perelman LT, et al —** Detection of Preinvasive Cancer Cells. Early-Warning Changes in Precancerous Epithelial Cells Can Now be Spotted In Situ. *Nature 2000;406,6791:35-36.*
2. **Wallace M, Perelman LT, Backman V, et al —** Endoscopic Detection of Dysplasia in Patients With Barrett's Esophagus Using Light Scattering Spectroscopy: A Prospective Study. *Gastroentorolgy 2000;119:677-82.*
3. **Yang C, Perelman LT, Wax A, et al —** Considerations for Field Based Light Scattering Spectroscopy. *J. Biomed. Opt. 2000;5:138-43.*
4. **Chen K, Perelman LT, Zhang Q, et al —** Optical Computed Tomography in a Turbid Medium using Early Arriving Photons. *J. Biomed. Opt. 2000;5:144-54.*
5. **Kneipp K, Kneipp H, Corio P, et al —** Surface-Enhanced and Normal Stokes and Anti-Stokes Raman Spectroscopy of Single-Walled Carbon Nanotubes. *Phys. Rev. Lett. 2000;84:3470-3.*
6. **Dark ML, Perelman LT, Itzkan I, et al —** Physical Properties of Hydrated Tissue Determined by Surface Interferometry of Laser-Induced Thermoelastic Deformation. *Phys. Med. Biol. 2000;45:529-539.*
7. **Gurjar R, Backman V, Perelman LT, et al.** Functional Imaging of Epithelial Tissues with Polarized Light Scattering Spectroscopy. *Nature Medicine 2001;7:1245-48.*
8. **Georgakoudi I, Jacobson BC, Van Dam J, et al —** Fluorescence, Reflectance and Light Scattering Spectroscopies for Evaluating Dysplasia in Patients with Barrett's Esophagus. *Gastroentorolgy 2001;120:1620-9.*
9. **Backman V, Perelman LT, Arendt JT, et al —** Light Scattering Spectroscopy: A New Technique for Clinical Diagnosis of Precancerous and Cancerous Changes in Human Epithelia. Las. *Life Sci. 2001; 9, 255-263.*
10. **Kneipp K, Perelman LT, Kneipp H, et al.** Coupling and Intensity Exchange Between Phonon Modes Observed in Strongly Enhanced Raman Spectra of Single-Wall Carbon Nanotubes on Silver Colloidal Clusters. *Phys. Rev. B 2001; 63:6319.*
11. **Anderson RR, de Boer J, Jacques SL, Perelman LT, Rajadhyaksha M, Tromberg B —** Optical Diagnostic Imaging Workshop, *Lasers in Surgery and Medicine 2003;32:246-46.*
12. **Fang H, Ollero M, Vitkin E, Kimerer LM, Cipolloni PB, Zaman MM, Freedman SD, Bigio IJ, Itzkan I, Hanlon EB and Perelman LT —** Noninvasive Sizing of Subcellular Organelles with Light Scattering Spectroscopy. *IEEE J. Sel. Top. Quant. Elect. 2003;9,2*
13. **G. Schuele, E. Vitkin, P. Huie, H. Fang, D. Palanker, and L.T. Perelman —** Optical Spectroscopy Non-Invasively Monitors Reaction of Subcellular Organelles to Cellular Stress. *Submitted to Nature Medicine.*
14. **H. Fang, M.M. Zaman, E. Vitkin, L.M. Kimerer, P.B. Cipolloni, I. Itzkan, S.D. Freedman, E.B. Hanlon and L.T. Perelman —** Confocal Light Scattering Spectroscopy can Nondestructively Detect Individual Subcellular Organelles. *To be submitted to Nature Biotechnology.*
15. **Perelman LT and Backman V —** Chapter XII. Light Scattering Spectroscopy of Epithelial Tissues: Principles and Applications. *In: Tuchin V, editor. Handbook on Optical Biomedical Diagnostics. Bellingham: SPIE Press; 2002, p.675-724.*
16. **Perelman LT, Modell MD, Vitkin E, Hanlon EB —** Light Scattering Spectroscopy: From Elastic to Inelastic *In: Tuchin V, editor Coherent-Domain Optical Methods For Biomedical Diagnostics, Environmental And Material Science. Kluwer Academic Publishers; (in press).*
17. **Backman V, Gurjar R, Perelman LT, et al —** Imaging and Measurement of Cell Organization with Submicron Accuracy Using Light Scattering Spectroscopy. *In: Optical Biopsy IV, Alfano RR, ed., Proceedings of SPIE, 2002; 4613:101-110.*
18. **Hanlon EB, Vitkin EI, and Perelman LT —** Light Scattering Spectroscopy Detects Changes in Alzheimer's Brain. *In: Biomedical Optical Spectroscopy and Diagnostics. Volume 22, Trends in Optics and Photonics Series. 2002; 387-389.*
19. **Perelman LT, Vitkin E, Fang H, Itzkan I —** Spectroscopic and Light Scattering Diagnostic Techniques. *In: IQEC 2002 Technical Digest, 2002; 262.*
20. **Hanlon EB, Siwek DF, Mckee AC, Kowall NW, Fang H, Vitkin EI, Perelman LT —** Optical Spectroscopy to Diagnose Alzheimer's Disease In Vivo. *In: Biomedical Optical Spectroscopy and Diagnostics. Trends in Optics and Photonics Series. 2004 (in press).*
21. **Fang H, Vitkin E, Ollero M, Itzkan I, Hanlon EB, Perelman LT —** Light Scattering Spectroscopy for Measuring Subcellular Organelles. *In: Biomedical Optical Spectroscopy and Diagnostics. Trends in Optics and Photonics Series. 2004 (in press).*
22. **Schuele IV G, Huie P, Vankov A, Vitkin E, Fang H, Hanlon EB, Perelman LT, Palanker D** Noninvasive Determination of Temperature-Induced Sub-Cellular Changes in RPE Using Light Scattering Spectroscopy *In: Ophthalmic Technologies XIV, Proceedings of SPIE, 2004 (in press).*

Patient Safety / Health Care Quality Research

Patient safety is one of the greatest challenges facing our health care system. According to the Institute of Medicine Report (published in 2000), between 44,000 and 98,000 deaths occur in hospitals in the United States every year due to adverse events. It is our moral obligation to improve the safety of childbirth and in the process we can reassure the public and our legislatures. This gives us a stronger argument for tort reform In 2002, funded by the Department of Defense and Harvard's Risk Management Foundation, we adapted the principles of Crew Resource Management (team training). The concept of Crew Resource Management (CRM) originated in the airline industry and all three branches of the military service. The implementation of these methods in the BIDMC labor and delivery unit was a first in the practice of obstetrics, and one of the first times ever in medicine. We have just completed a 15-hospital randomized control trial with the objective of proving that this approach can improve patient safety. Since the introduction of CRM at BIDMC, we have noted a dramatic improvement in patient safety, while simultaneously noting a dramatic rise in patient and staff satisfaction. We believe that team training is effective, especially

when built on a solid base of quality assurance and quality improvement programs. The evaluation and adoption of team training has dramatically affected the culture of safety in our department of obstetrics. As a result of our leadership role in this field, we have begun to see the concepts of team training applied to other areas of health care, including emergency departments, operating rooms and intensive care units.

PREECLAMPSIA / HYPERTENSIVE DISORDERS OF PREGNANCY

S. Ananth Karumanchi, M.D.
Assistant Professor in Medicine and Obstetrics and Gynecology, Harvard Medical School

Dr. Karumanchi's current research focuses on the role of angiogenic growth factors and inhibitors in the pathogenesis of placental disorders such as preeclampsia, and IUGR. NIH and the American Society of Nephrology currently fund his research. His work has resulted in a dramatic advance in our understanding of the pathogenesis of preeclampsia and potential new therapies.

Research Projects

Role of sFlt-1 in the pathogenesis of preeclampsia — Identification and characterization of sFlt-1 (a circulating VEGF antagonist) as a potential mediator of the clinical phenotype of preeclampsia; Creation of a novel animal model for preeclampsia and studying the effects of therapeutic compounds such as PlGF, VEGF, nicotine in this animal model.
Funded by: American Society of Nephrology – $100,000

Role of TGF-beta in VHL-associated renal cancer — Identification and characterization of the TGF-beta 1 mRNA binding proteins regulated by VHL tumor suppressor; Characterization of pregnancy associated plasma protein-1 as a novel target for VHL tumor suppressor and its role in placental development and intra-uterine growth retardation.
Funded by: NIH/NIDDK$126,000

Placental gene expression profile in preeclampsia — Gene expression profile from preeclamptic and normal placentas performed using affymetrix microarrays; Goals will be to identify novel secreted factors which can be used for the early diagnosis of preeclampsia and which may play a role in the pathogenesis of preeclampsia.
Funded by: NIH/NIDDK – $74,500

Angigogenesis-related gene products in preeclampsia — Defining the role of VEGF, PlGF and sFlt-1 in the pathogenesis of preeclampsia using in vitro cell culture and in vivo angiogenesis assays; To study the regulation of sFlt-1 gene product in trophoblasts exposed to hypoxia.
Funded by: NIH/NICHD – $325,500

Related Publications

Maynard SE, Min J, Merchan J, Lim KH, Li J, Mondal S, Libermann T, Morgan JP, Sellke FW, Stillman IE, Epstein FH, Sukhatme VP, Karumanchi SA — Excess Placental sFlt-1 May Contribute to Endothelial Dysfunction, Hypertension and Proteinuria in Preeclampsia.
Journal of Clinical Investigation 2003, 111:649-658.

Thadhani RI, Mutter W, Wolf M, Levine R, Taylor RN, Sukhatme VP, Ecker J, Karumanchi SA — First Trimester Soluble Fms Like Tyrosine Kinase-1 and Placental Growth Factor and Risk for Pre-eclampsia. *Journal of Clinical Endocrinology and Metabolism 2004, 89: 770-75.*

Levine RJ, Maynard SE, Qian C, Lim KH, England LJ, Yu KF, Schisterman EF, Thadhani RI, Sachs BP, Epstein FH, Sibai BM, Sukhatme VP, Karumanchi SA — Circulating Angiogenic Factors and the Risk for Preeclampsia.
New England Journal of Medicine 2004, 350:672-83.

Thadhani R, Ecker JL, Mutter WP, Wolf M, Smirnakis KV, Sukhatme VP, Levine RJ, Karumanchi SA — Insulin Resistance and Alterations in Angiogenesis: Additive Insults That May Lead to Preeclampsia. *Hypertension 2004, 43(5):988-92*

Kang DH, Finch J, Nakagawa T, Karumanchi SA, Kanellis J, Granger J, Johnson RJ — Uric Acid, Endothelial Dysfunction and Preeclampsia: Searching for a Pathogenetic Link.
Journal of Hypertension 2004, 22:229-235

Davison JM, Homuth V, Jeybalan A, Conrad KP, Karumanchi SA, Quaggin S, Dechend R, Luft F — Current Ideas on Preeclampsia.
Journal of the American Society of Nephrology, In Press, 2004

Lam C, Lim, KH, Kang D, Karumanchi SA — Uric Acid and Preeclampsia.
Seminars in Nephrology, In Press 2004

REPRODUCTIVE ENDOCRINOLOGY / BOSTON IVF

Richard H. Reindollar, M.D.
Associate Professor, Harvard Medical School;
Director, Division of Reproductive Endocrinology

Dr. Richard H. Reindollar earned his medical degree from the Bowman Gray School of Medicine in Winston Salem, NC. He completed his residency in obstetrics and gynecology at York Hospital, York, PA, and completed a fellowship in reproductive endocrinology and genetics at Medical College of Georgia, Augusta, GA. He is the director of the division of reproductive endocrinology at BIDMC and an associate professor of obstetrics, gynecology and reproductive biology at HMS. Dr. Reindollar has been awarded numerous citations for excellence in teaching and is the past-president of the Society of Reproductive Endocrinologists, and New England Fertility Society. He is also a founding fellow of the American College of Medical Genetics, a past-president of the North American Society for Pediatric and Adolescent Gynecology, and a member of many other professional organizations. He has published a great number of articles in professional medical journals, as well as abstracts and invited book chapters, and has lectured extensively at postgraduate courses and seminars.

The goals of the reproductive endocrinology and infertility research lab have been to study major genes and pathways involved in reproduction. We have directed a major effort towards understanding molecular pathways involved in ovarian function. We are applying basic biochemical, physical, and structural analyses together with clinical research to search for molecular markers of follicular selection/ recruitment and ovarian aging.

For many years the laboratory was focused on the study of patients with congenital absence of the uterus and vagina (CAUV) in order to identify genes involved in development of the mullerian system.

Current Major Research Focus

A woman's ability to conceive depends on the supply of oocytes, their quality and ovarian functionality. This declines dramatically with aging and beyond age 40 years female fertility is nearly lost. The reproductive failure of the aging ovaries may be related to structural and functional ovarian alterations in addition to follicular depletion. Although the woman's infertility is the focus of major problems in the female population at age above 38 years and ovarian dysfunction is a frequent cause of infertility, the molecular mechanisms underlying this ovarian dysfunction are poorly understood.

Based on our previous study showing age-associated changes at RNA and protein levels in rodent tissues, we believe that the profound decline in ovarian function is marked by altered gene expression and the protein profile. To test this hypothesis, we are comparing the gene expression profile applying DNA array analyses on gene libraries from young and retired female mouse breeders. We are establishing a mouse-specific ovarian DNA array for routine analyses of aging related genetic ovarian changes. We are searching for fertility- and infertility-specific ovarian phenotypes as a function of ovarian aging and reproductive ovarian functionality.

We are mapping the protein-network to determine how proteins interact with each other in relation with aging and infertility. It is these interactions that determine the function of signal-transduction cascades, global and gene-specific transcription regulation in response to ovarian aging. Protein-network profiling will help to assess the status of all known and unknown participants in pathways that are responsive to ovarian aging.

We are identifying how proteins are modified in response to ovarian aging. Several posttranslational protein modifications such as acetylation, O-glycosylation, ubiquitination, sumolation govern the structure, function, protein turnover, cellular localization (figure 1) and migration of proteins. We also applying a variety of analytical methods to identify age-dependent modified proteins and the nature of the modification.

This information has tremendous applications for detecting potential protein targets for drug therapy of age related ovarian dysfunction and infertility that are Independent of the normal loss of germ cells or related to premature germ cell loss. In addition, we are searching for non-invasive nanotechnology-based physical methods to predict follicular quality based on changes in the electronic futures of the follicular fluid.

DIVISION OF REPRODUCTIVE ENDOCRINOLOGY / BOSTON IVF

Research Projects

Optimal Infertility Therapy RCT: Women 40 and Older — Randomized controlled trial to identify the most effective infertility treatment for couples from the 40th birthday of the female partner to the 43rd birthday. Parameters followed include cost effectiveness, success rates, adverse outcomes. Funded by: NIH – $2.7 million / 5 years

Conventional Infertility Therapy vs. A Fast Track to IVF — Randomized controlled trial of a standard infertility paradigm compared to a fast track to IVF for couples up to the female partner's 40th birthday. Parameters followed include cost effectiveness, success rates, adverse outcomes. *Funded by: NIH – $2.7 million / 5years*

Molecular Basis of Congenital Absence of the Uterus and Vagina (CAUV) — Use of a number of molecular strategies to identify molecular basis of CAUV and determine the genes involved in development of the mullerian system. Research is designed to identify both germline and somatic cell mutations. *Funded by: Industry – $10,000 (Organon), $2,000 (Ferring)*

Gene expression profiles of human ovarian granulosa cells in young and aged women undergoing in vitro fertilization — The purpose of this study is to identify and describe differential gene expression profiles in the granulosa cells of women undergoing IVF who are of varying age and have variable responses to ovulation induction.
Funded by: Industry – $10,000 (Serono)

Development of stem cell lines from donated cryopreserved embryos — A collaborative study between Boston IVF and Department of Biology, Harvard University, to develop stem cell lines from donated cryopreserved embryos. *Funded by: Howard Hughes foundation, Prof. Doug Melton, Harvard University – $100,000 a year for 6yrs.*

Hyperstimulation for In Vitro Fertilzation — A Randomized Quality of Life, Efficacy, Safety, and Tolerability (QUEST) Study of Bravelle + Repronex, vs Gonal-F in Controlled Ovarian Hyperstimulation for In Vitro Fertilzation. Primary Investigator - Alan S. Penzias, M.D.
Funded by: Ferring Pharmaceuticals

Cryopreservation of Human Oocytes followed by Post-Thaw Evaluation of Survival — A Collaborative study between Boston IVF, ViaCell Inc, and Gamete Technology Inc. Investigators - R. Douglas Powers Ph.D., Michael Alper M.D.

Original Articles

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Klipstein S, Reindollar RH, Regan M Alper MM — Gender Bias in the Disposition of Frozen Embryos. *Fertil Steril 2001; 76(6):1181-1184*

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Timmreck LS, Gray MR, Handelin B, Allito B, Rohlfs E, Davis AJ, Gidwani G, Reindollar RH — Analysis of Cystic Fibrosis Transmembrane Conductance Regulator Gene Mutations in Patients With Congenital Absence of the Uterus and Vagina. *Amer J Med Gen July 2003; 120A(1):72-76*

Klipstein S, Bhagavath B, Topipat C, Sasur L, Reindollar RH, Gray MR — The N314D Polymorphism of the GALT Gene is Not Associated with Congenital Absence of the Uterus and Vagina (CAUV). *Molec Human Reprod 2003;9(3):171-74.*

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Klipstein S, Reindollar RH, Regan MM, Alper MM — Initiation of the Gonadotropin-Releasing Hormone Antagonist Ganirelix for In Vitro Fertiliation Cycles in Which the Lead Follicle is >14 mm. *Fertil Steril, 2004; 81(3):714-71*

Selected Abstracts

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Lalwani SI, Friedman R, Timmreck LJ, Harris D, Penzias AS, Reindollar RH — Beth Israel Deaconess Medical Center, Harvard Medical School, Boston IVF. What Does the SART Success Rate for a Given IVF Program Mean? ASRM, Orlando, Florida. *Fertil Steril 2001;74(3S) Suppl:S250*

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Lalwani S, Berger M, Klipstein S, Timmreck L, Gardella J, Reindollar R — Gestational Surrogacy: A Model to Study the Maximum Success Rates Offered by an IVF Program [abstract P-83]. ASRM, Seattle, Washington. *Fertil Steril 2002;76(3S) Suppl:S143*

Wu HH, Reindollar RH, Gray MR — Analysis of the WNT-4 Gene in Women With Congenital Absence of the Uterus and Vagina [abstract P-161]. ASRM, Seattle, Washington. *Fertil Steril 2002;76(3S) Suppl:S169*

Klipstein S, Harris DH, Alper MM, Ryley DA, Timmreck L, Reindollar RH — Success Rates in Women Undergoing In Vitro Fertilization (IVF) at Age 40 and Above at the Nation's Largest IVF Center. *Washington DC. J Soc Gynecol Inves 2003;10(2) Suppl:286A*

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Ryley DA, Wu HH, Zimon AE, Reindollar RH, Gray MR — Characterization of the Human FORMIN2 (FMN2) Gene and Analysis of the FMN2 Gene in Patients With Unexplained Infertility. [abstract 184]. *Houston, Texas. J Soc Gynecol Inves 2004;11(2) Suppl:132A*

Zimon AE, Oellinger R, Ryley DA, Reindollar RH, Usheva A — Gene Expression Profiling of Young and Aged Mouse Ovaries. [abstract 615]. *Houston, Texas. J Soc Gynecol Inves 2004;11(2) Suppl:281A*

Reviews, Chapters, and Editorials

Seifter DB, Dodson WC, Reindollar RH, Santoro NF — Curbing High Order Multiple Births, A Panel Discussion. *Contemp OB/GYN 2001;46(2):57-83*

Reindollar RH — Should we Consider Twins a Success in OI or ART? No. *Contemp OB/GYN 2002; 47(9):44-61*

Lalwani S, Reindollar RH, Davis AJ — Normal Onset of Puberty - Have Definitions of Onset Changed? *In: Davis A, editor. Infertility and Reproductive Medicine Clinics of North America, Vol 14. USA: Elsevier Science; 2003. p. 29-36*

Timmreck L, Reindollar RH — Contemporary issues in primary amenorrhea. *In: Davis AJ, editor. Infertility and Repro. Medicine Clinics of N. America, Vol.14. , USA: Elsevier Science; 2003. p. 37-52*

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RESEARCHERS

Michael M. Alper, M.D.

Dr Michael M. Alper, assistant professor, obstetrics, gynecology and reproductive biology, Harvard Medical School, and medical director at Boston IVF, has been in practice for more than 25 years, joining Boston IVF in 1986. Board Certified in reproductive endocrinology by the American Board of Obstetrics and Gynecology, Dr. Alper received his medical degree from McGill University, Montreal, Quebec. He fulfilled his residency at Harvard Medical School, Beth Israel Hospital, Boston, MA where he also completed his fellowship in reproductive endocrinology and infertility. Dr. Alper is on staff at Nantucket Cottage Hospital, Surgery Center of Waltham, Newton-Wellesley Hospital, and Beth Israel Deaconess Medical Center.

Dr. Alper is an assistant clinical professor at HMS. His interest of in vitro fertilization has led him to be involved in specific research studies including NIH-funded "FAST TRACK STUDY", and privately funded, industry sponsored clinical trials. Dr. Alper has published extensively and has written articles, abstracts, letters and books. In the past two years he has lectured all over the world, from Argentina to Canada to Japan. Dr. Alper has co-authored several books. His latest book, "Quality Management Systems for Assisted Reproductive Technologies: ISO 9001:2000" has just been published by Taylor & Francis.

Research

- Oocyte freezing project using injection of trehalose
- Clinical trial of Oral Contraceptive pre-treatment in antagonist IVF cycles

Yuval Bdolah M.D., M.Sc

Research Fellow and Instructor of OB/GYN, Harvard Medical School

Recent Research Projects (2001 – present)

- A project concerning trophoblast cell lines, examining the expression of endothelial markers of these cells, as related to the differentiation process along an invasive lineage (an abstract on this topic was recently presented at the annual Society of Gynecolgic Research – SGI - meeting).
- The effect of sFlt-1 on the clinical symptoms in rats, in a preeclampsia model. I am injecting sFlt-1 in an adenovirus system to pregnant rats and examining the phenoptype in correlation to the effects on the placenta.
- A project in collaboration with the reproductive endocrinology division of the department of OB/GYN (headed by Dr. Reindollar) and the Boston IVF: a clinical trial in order to examine the impact of angiogenesis on the implantation process. We intend to check the angiogenesis state in recurrent implantation failures of IVF patients.
- A study that examines the angiogenesis status and placentas of pregnant patients with fetal chromosomal aberrations, and a higher risk of developing preeclampsia.
- A study that examines the angiogenesis status in twin pregnancies.
- A study that examines the angiogenesis status in infertile patients that developed preeclampsia, later on.

Funding

2003-2004 — $5000 fellowship grant from The American Physician Fellowship For Medicine In Israel

Publications

Farhat M., Zentner B., Lossos F., Bdolah Y., Holtzer H., and HurwitzA—Successful pregnancy following replacement of embryos previously refrozen at blastocyte stage. *Hum. Reprod. 2001;16(2):337-339*

Dr. Bdolah is a physician-scientist who is spending two years at Harvard/ Beth Israel Deaconess Medical Center as a research fellow in the departments of obstetrics and gynecology and renal division. He received his medical degree in 1991 from Hadassah – Hebrew University Medical School, Jerusalem, Israel, and a M.Sc. in neurobiology from the same institution in 1992. Following his medical training, he completed a residency and fellowship in obstetrics and gynecology, specializing in reproductive endocrinology.

Dr. Bdolah has joined a collaborative effort between the departments of nephrology, pathology, surgery and obstetrics and gynecology at BIDMC to unravel the pathphysiology of preeclampsia. Headed by Dr. Ananth Karumanchi from the renal division and the department of obstetrics and gynecology, this team has found the probable cause of preeclampsia; furthemore, there is an exciting potential new diagnostic tool and therapy. Dr. Bdolah's focus is on the molecular and genetic mechanisms underlying the defective trophoblast behavior seen in preeclamptic placentas.

Deborah Levine, M.D.

Dr. Deborah Levine is an associate professor of radiology at Harvard Medical School, co-chief of ultrasound and director of OB/GYN ultrasound. Dr. Levine's research interest is improving prenatal diagnosis with use of obstetric MRI. She has an NIH R01 grant entitled "MRI of Fetal Ventriculomegaly: Morphology and Outcome."

Research Projects

MRI of Fetal Ventriculomegaly: Morphology and Outcome — This grant evaluates fetal CNS anomalies on MRI compared with ultrasound, and correlates imaging findings with postnatal outcomes. *Funded by: NIH – $450,000*

Placental oxygenation and perfusion imaging with MRI — This grant is being used to develop sequences that will detect blood flow changes in the normal and abnormal placenta, using a sheep model of placental insufficiency. *Funded by: NIH – 70,000*

Parallel and real-time MR imaging of the fetus - what imaging parameters work best?— These projects compare our baseline fast MR imaging with new techniques that allow for faster (and possibly better) imaging. *Funded by: None – plan is for NIH grant to be submitted*

MR of RLQ pain in pregnancy — Patients with suspected appendicitis with nondiagnostic sonograms are being referred for MR. In this project we evaluate MR visualization of appendix and associated pathology. *Funded by: None*

Related Recent Publications

Levine D, Mehta TS, Min KK, Hulka, CA, McArdle CR — Technical Factors Influencing Visualization of a Fetal Echogenic Intracardiac Focus. *J Clin Ultrasound, 2000;28:479-484*

Levine D, Barnes PB, Korf B, Edelman RR — Tuberous Sclerosis: Second Trimester Diagnosis of Subependymal Tubers with Fast *MRI. AJR, 2000; 175:1067-1069*

Choi JR, Levine D, Finberg H — Luteoma of Pregnancy: Sonographic Findings in Two Cases. *J Ultrasound Med, 2000;19:887-891*

Trop I, Levine D. Hemorrhage during pregnancy — Sonography and MR Imaging. *AJR, 2001;176:607-615*

Rosen M, Mehta TS, Bromberg R, Kelly SL, Levine D — Remote Ultrasound Interpretation Using a Laser Printer Network: System Performance and Diagnostic Accuracy, in Actual Clinical Practice. *AJR, 2001; 176:855-860*

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Levine D, Jennings R, Barnewolt C, Mehta T, Wilson J, Wong G — P rogressive Fetal Bronchial Obstruction Caused by a Bronchogenic Cyst Diagnosed by Prenatal MR Imaging. *AJR, 2001;176:49-52*

Folkerth R, McLaughlin M, Levine D — Organizing Posterior Fossa Hematomas Simulating Developmental Cysts on Prenatal Imaging: Report of Three Cases. *J Ultrasound Med, 2001: 20:1233-1240*

Morof D, Levine D, Stringer K.F., Grable I, Folkerth R — P renatal Diagnosis of Glioblastoma Multiforme. *J Ultrasound Med, 2001; 20:1369-1375*

Monsky W, Levine D, Mehta TS, Kennedy B, Kane R, Nissenbaum H — Using an Ultrasound Simulator to Prepare Residents for Night Call. *AJR, 2002; 178:35-39*

Levine D, Trop I, Mehta T, Barnes PD — MR Appearance of Fetal Cerebral Ventricular Morphology. *Radiology, 2002; 223:652-660*

Siewert B, Hochman M, Levine D — MRI Findings of Congenital Anomalies of the Uterus: Causes for Inaccurate Classification. *Journal of Women's Imaging, 2002; 4:100-107*

Levine D, Barnewolt CE, Mehta TS, Trop I, Estroff J, Wong G — Fetal Thoracic Abnormalities: Magnetic Resonance Imaging.*Radiology, 2003;228:379-388*

Levine D, Barnes PD, Robertson RR, Wong G, Mehta TS — Fast MRI of Fetal CNS Abnormalities.*Radiology, 2003;229:51-61*

Stroustrup Smith A, Estroff J, Barnewolt C, Levine D — Prenatal Diagnosis of Cleft Lip and Cleft Palate by Magnetic Resonance Imaging. *AJR, 2004;183:229-235*

Eyvazzadeh A, Pedrosa I, Rofsky N, Seiwert B, Farrar N, Abbott J, Levine D — MRI of Right Lower Quadrant Pain in Pregnancy. *AJR, in press*

Chiang G, Levine D, Mehta TS, McNamara A — The Intradecidual Sign: A Reliable Marker for Intrauterine Pregnancy. *AJR, in press*

McKenzie C, Levine D, Farrar N, Dialani V, Rofsky N — ASSET Enhanced SSFSE Imaging of the Fetus. *Proceedings of the International Society for Magnetic Resonance in Medicine XVII, 2004*

McKenzie C, Levine D, Farrar N, Dialani V, Rofsky N — R e a l - Time Imaging of the Fetus. *Proceedings of the International Society for Magnetic Resonance in Medicine XVII, 2004*

Stroustrup Smith AS, Levine D — Development of Interhemispheric Cyst Associated with Agenesis of the Corpus Callosum. *AJNR, 2004:25:1037-1040*

Morof D, Grable I, Fishman S., Jennings R, Barnewolt C, Estroff J, R Rabar, Levine D — Oropharyngeal Teratoma: Prenatal Diagnosis and Assessment Using Ultrasound, MRI, and CT with Management by EXIT Procedure. *AJR, 2004:183:493-496*

Levine D, Stroustrup Smith A, McKenzie — Tips and Tricks of Fetal MRI. *Radiologic Clinics of North America, 2003;41:729-746*

Levine D — Fetal Magnetic Resonance Imaging. *J Maternal-Fetal & Neonatal Medicine, 2004;15:85-94*

Chiang G, Levine D — Imaging of Ovarian Masses in Pregnancy. *J Ultrasound Med, 2004;23:805-819*

Swire MN, Castro-Aragon I, Levine D — Various Sonographic Appearances of the Hemorrhagic Corpus Luteum Cyst. *Ultrasound Quarterly, 2004; 20:45-58*

Rahbar R, Vogel A; Myers LB, Bulich LA, Wilkins-Haug L; Benson CB, Grable IA, Levine D, Fishman SJ, Jennings RW, Estroff JA, Barnewolt CE — A New Era in Diagnosis and Management of Fetal Airway Obstruction Due to Advances in Prenatal Imaging. *Archives of Otolaryngology-Head&Neck Surgery, in press*

Mehta T, Levine D — Imaging of Fetal Cerebral Ventriculomegaly - A Guide to Management and Outcome. *Seminars in Neonatology, in press*

Kee-Hak Lim, M.D.

In collaboration with nephrology, we have been involved in investigating the role of angiogenic factors in preeclampsia. We have shown that soluble form of vascular endothelial growth factor receptor type I (sVEGFR-1) plays an important role in development of hypertension, proteinuria and glomerular endotheliosis noted in preeclampsia. In addition, we showed that a rise in sVEGFR-1 and a decrease inplacental growth factor level in serum precede the on set of symptoms of preeclampsia. We are currently investigating not only the role of sVEGFR-1, PlGF and VEGF in the pathogenesis of preeclampspia, but also their role in placental development, as well as their diagnostic utility. More importantly, we are investigating various therapeutic approaches using molecules that can counter sVEGFR-1 in preeclampsia. Our work is funded by NIH, Scios and the Obstetrics and Gynecology Research Foundation at BIDMC.

Publications

Levine RJ, Maynard SE, Qian C, Lim KH, England LJ, Yu KF, Schisterman EF, Thadhani R, Sachs BP, Epstein FH, Sibai BM, Sukhatme VP — Circulating Angiogenic Factors and the Risk of Preeclampsia. *New England Journal of Medicine. 2004 Feb 12;350(7):672-83*

Hamar BD, Levine D, Katz NL, Lim KH — Expectant Management of Uterine Dehiscence in the Second Trimester of Pregnancy. *Obstetrics and Gynecology. 2003 Nov;102(5 Pt 2):1139-42*

Maynard SE, Min JY, Merchan J, Lim KH, Li J, Mondal S, Libermann TA, Morgan JP, Sellke FW, Stillman IE, Epstein FH, Sukhatme VP, Karumanchi SA — Excess Placental Soluble fms-Like Tyrosine Kinase 1 (sFlt1) May Contribute to Endothelial Dysfunction, Hypertension and Proteinuria in Preeclampsia. *J Clin Invest. 2003 Mar;111(5):649-58. PMID: 12618519*

Alan S. Penzias, M.D.

Dr. Alan S. Penzias earned a bachelors degree in chemistry cum laude from the University of Pennsylvania. His undergraduate research and thesis in chemistry was performed under the direction of Professor Alan G. MacDiarmid, recipient of the 2000 Nobel Prize in chemistry.

Dr. Penzias received his medical degree from the State University of New York - Downstate Medical Center in Brooklyn, New York. He went on to complete a residency in obstetrics and gynecology at Beth Israel Hospital, Harvard Medical School, Boston, Massachusetts and from there, a fellowship in reproductive endocrinology at Yale University, in New Haven, Connecticut under the direction of his mentor, Professor Alan DeCherney. Dr. Penzias was an instructor at Yale University School of Medicine and in 1992 became and assistant professor of obstetrics and gynecology at Boston's Tufts University School of Medicine, where he then became the director of its in vitro fertilization program.

In 1996, Dr. Penzias was appointed an assistant professor of obstetrics, gynecology and reproductive biology at HMS, the same year he joined Boston IVF, one of the United States' largest infertility centers. He also serves as the associate director of the division of reproductive endocrinology and infertility at BIDMC and HMS in Boston.

In 2000 he served as president of the New England Fertility Society and served for three years on its board of directors. Dr. Penzias' commitment to patient advocacy is manifest in serving as a member of the board of directors of Boston-based Triplets Moms and More, and the New York-based, nationally and internationally renowned patient advocacy group American Infertility Association. Dr. Penzias' professional experience, expertise and research have focused on the "patient-friendly" approach to infertility treatment. Removing barriers to care through innovation and outcomes oriented research. He is a co-investigator and member of the steering committee on America's largest National Institutes of Health-funded infertility treatment grant, the FASTT Trial, which is spearheaded by Dr. Richard Reindollar.

Dr. Penzias' early research in ART began with studies of the GIFT procedure. He published a suite of papers on the decline in success rates with advancing age and the optimal number of oocytes to transfer along with simplification of the technique by examining the impact of unilateral or bilateral tubal transfer. He conducted one of the first prospective randomized trials of GnRH agonists for use in IVF, a study that was selected as a prize paper by the American College of Obstetricians and Gynecologists.

Other publications have been aimed at the optimization of stimulation parameters and conditions in ART. These included the impact of baseline ovarian cysts prior to gonadotropin stimulation, the predictive value of early pituitary suppression on IVF outcome; sonographic follicular size and shape on oocyte maturity and fertilization rates; and corpus luteum life span and luteal phase support following ART. He has co-authored studies of granulosa cells obtained at egg retrieval using flow cytometry to evaluate the impact of age and stimulation regimen on cell cycle parameters. In addition he has co-authored studies of eggs that failed to fertilize following ICSI with biochemical evaluation of their zona pellucidae and decondensation patterns of their maternal and paternal chromatin; as well as the technical and physiological aspects associated with the lower fertilization rates following ICSI. He has also studied the adverse impact of ART with respect to multiple pregnancy co-authoring papers on the costs, neonatal morbidity and mortality of triplet pregnancy.

Dr. Penzias has been awarded numerous citations for excellence in teaching and has been named one of Boston's best doctors in Boston Magazine's "Best of Boston 2003". He recently received a citation as one of the "Best Doctors in America" 2003-2004 by Best Doctors® a distinction of the top 5% of doctors selected by their peers in 400 medical specialties. Dr. Penzias has more than 65 peer-reviewed publications and textbook chapters to his credit. He has been a featured lecturer at numerous professional seminars nationally and internationally. He serves as an ad hoc editor for a number of professional publications, including The New England Journal of Medicine and Fertility and Sterility. His list of professional society memberships includes the American Society for Reproductive Medicine, the Society of Reproductive Endocrinology and Infertility and the American College of Obstetricians and Gynecologists.

Research Grants

2001 A randomized, comparative, 3 arm parallel group, open-label multicenter study of the efficacy and safety of purified human FSH SC and Repronex SC when combined in continuous or sequential dose ratios in female patients 18-33 undergoing IVF. Co-Investigator. *Funded by: Ferring Laboratories – $50,000*

2001 A multicenter, open label pilot study to assess the efficacy and convenience of Antagon treatment following pre-treatment with the oral contraceptive pill Desogen for scheduling, in women undergoing controlled ovarian hyperstimulation. Co-Investigator. *Funded by: Organon Inc.. – $50,000*

2003 A Randomized Quality of Life, Efficacy, Safety Tolerability (QUEST) Study of Bravelle vs. Gonal-F in Controlled Ovarian Hyperstimulation for In Vitro Fertilization. Principal Investigator. *Funding: – $50,000*

Publications

Schwartz LB, Naftolin F, Lyttle CR, Penzias AS, Meaddough EL, Kliman HJ — Mouse Ascites Golgi (MAG) Mucin Expression and Regulation by Progesterone in the Rat Uterus. *J Soc Gynecol Invest 8:216-23; 2001*

Penzias AS — Luteal Phase Support. *Fertil Steril 77:318-23; 2002*

Penzias AS — When Does the Dream Die? Or Does it? *Fertil Steril. 81:274-5; 2004*

Lalwani S, Timmreck L, Friedman R, Penzias A, Alper M, Reindollar RH — Variations in Individual Physician Success Rates Within an In Vitro Fertilization Program Might Be Due to Patient Demographics. *Fertil Steril 81:944-6; 2004*

Lalwani S, Timmreck L, Friedman R, Penzias A, Alper M, Reindollar RH — Variations Within an In Vitro Fertilization Program Might Be Caused by Patient Demographics. *Fertil Steril, 2004;81(4): 952-953*

Penzias AS — Improving Results with Assisted Reproductive Technologies: Individualized Patient Tailored Strategies for Ovulation Induction. *Reproductive Biomedicine Online 2004; 9(1):43-6*

Garcia JE, Kettel LM, Klein NA, Odem RR, Penzias AS, Silverberg KM, Steinkampf MP, Young JE, Young P, Mahony M — An Aqueous Formulation of Recombinant Human FSH Is More Efficient Than a Freeze-Dried Cake Formulation in Clomiphene-Resistant Women with Chronic Anovulation. *Today's Therapeutic Trends 2004;22(3):147-165*

Penzias AS, Alper MM — Luteal Support with Vaginal Micronized Progesterone Gel in Assisted Reproduction. *Reprod Biomed Online 6:287-95, 2003*

Penzias AS — Book Review: Reproductive Medicine: Molecular, Cellular and Genetic Fundamentals. *JAMA 290:3005, 2003*

Dabney L, Penzias AS — Gamete Technologies. The Physiologic Basis of Obstetrics and Gynecology. Seifer DB, Samuels P, Kniss DA (Eds). *Philadelphia, Lippincott Williams & Wilkins. 2001*

Sinnock K, Penzias AS — Intratubal Transfer. In Office Based Infertility Practice. Seifer DB. Collins RL (Eds). *New York, Springer-Verlag. 2001*

Penzias AS, Perlmutter J. CPT — Coding Infertility Surgery. In OperativeGynecology.

Gershenson DM, DeCherney AH, Curry S, Brubaker L (Eds) — Philadelphia, WB Saunders, pages 33-6. 2001. **Penzias AS —** The Oocyte Complex. *In the Encyclopedia of Endocrine Diseases. Martini L (Ed). San Diego, Academic Press. 2004*

Lalwani SI, Friedman R, Timmreck LJ, Harris D, Penzias AS, Reindollar RH — What Does the SART Success Rate for a Given IVF Program Mean? Fertil Steril 76:S250-S251, 2001

Bayer S, Thornton K, Penzias A, Alper MM — Experience With the Use of a GnRH Antagonist in IVF Patients Who Are Poor Responders. *Fertil Steril 76:S235, 2001*

Domar AD, Nielsen B, Dusek J, Paul D, Penzias AS, Merari D — The Impact of Spirituality / Religiosity on Distress in Infertile Women. *Fertil Steril 76:S198, 2001*

Alper MM, Bayer SR, Lesser C, Penzias AS — Patient Friendly IVF: Initial Experience With a Modified GnRH Antagonist Protocol. *Fertil Steril 77:S22, 2002*

Anny Usheva-Simidjiyska, Ph.D.

Anny Usheva-Simidjiyska, Ph.D., director, basic science research, reproductive endocrinology, department of obstetrics and gynecology, Beth Israel Deaconess Medical Center, Harvard Medical School

Education and Training

Sofia Institute of Chemical Technology — M.S. in Chemistry, M.S. in Computational Programming

German Academy of Science, Berlin-Buch 1982 —Ph.D.

Weizmann Institute of Science, Rehovot, Israel 1992 — Gene transcription regulation

Princeton University, Princeton, Nj 1997 — Gene transcription initiation of basic and regulated transcription, protein, protein-DNA interactions, dynamics and three-dimensional structures.

Positions and Honors

1997	Assistant Professor, Harvard Medical School
2003	Visiting Scientist, Division of Theoretical Physics, Los Alamos National Laboratory
2004	Director of Basic Research, Reproductive Endocrinology, Department of Obstetrics & Gynecology, Beth Israel Deaconess Medical Center

Honors

1977	Special award from the Bulgarian Chemical Society
1985	Foreign fellowship award, Bulgaria
1985	Foreign fellowship, German Foundation for Academic Exchanges
1988	Research fellowship, Royal Swedish Academy of Sciences, Stokholm, Swiden
1989-1990	Research fellowship, Federation of European Biochemical Societies (FEBS)
1990-1991	Scholar in Life Sciences, Weizmann Institute of Sciences
1996	Teaching award, Princeton University
1998-2003	Edward Mallinckrodt Jr. research grant, Mallinckrodt Foundation
2000-2004	Young Investigator Award, American Heart Association
2004	Reviewer, Center for Integrated Nanotechnologies Study Section, Department of Energy
2004	Sandia/Los Alamos Integrated Nanotechnologies, Department of Energy, User Award

Peer-Reviewed Publications (2001 - 2004)

Kasahara, H., Usheva, A., Ueyama, T., Aoki, H., Horikoshi, N., and Izumo, S. (2001) — Characterization of Homo- and Heterodimerization of Cardiac Csx/Nkx2.5 Homeoprotein. *J Biol Chem 276, 4570-4580*

Liao, H. S., Kang, P. M., Nagashima, H., Yamasaki, N., Usheva, A., Ding, B., Lorell, B. H., and Izumo, S. (2001) — Cardiac-Specific Overexpression of Cyclin-Dependent Kinase 2 Increases Smaller Mononuclear Cardiomyocytes. *Circ Res 88, 443-450*

Petkova, V., Romanowski, M. J., Sulijoadikusumo, I., Rohne, D., Kang, P., Shenk, T., and Usheva, A. (2001) — Interaction Between YY1 and the Retinoblastoma Protein. Regulation of Cell Cycle Progression in Differentiated Cells. *J Biol Chem 276, 7932-7936*

Schinke, M., Litovsky, S., Usheva, A., Tanaka, M., Maguire, C., Berul, C., and Izumo, S. (2001) — Lack of the Conserved NK2-Domain of the Cardiac Transcription Factor Nkx2.5 Causes Multiple Heart Defects. *Circulation 104, 127 Suppl*

Sulijoadikusumo, I., Horikoshi, N., and Usheva, A. (2001) — Another Function for the Mitochondrial Ribosomal RNA: Protein Folding. *Biochemistry 40, 11559-11564*

Bodyak, N., Kang, P. M., Hiromura, M., Sulijoadikusumo, I., Horikoshi, N., Khrapko, K., and Usheva, A. (2002) — Gene Expression Profiling of the Aging Mouse Cardiac Myocytes. *Nucleic Acids Res 30, 3788-3794*

Ohiro, Y., Garkavtsev, I., Kobayashi, S., Sreekumar, K. R., Nantz, R., Higashikubo, B. T., Duffy, S. L., Higashikubo, R., Usheva, A., Gius, D., et al. (2002) — A Novel p53-Inducible Apoptogenic Gene, PRG3, Encodes a Homologue of the Apoptosis-Inducing Factor (AIF). *FEBS Lett 524, 163-171*

Soares, M. P., Usheva, A., Brouard, S., Berberat, P. O., Gunther, L., Tobiasch, E., and Bach, F. H. (2002) — Modulation of Endothelial Cell Apoptosis by Heme Oxygenase-1-Derived Carbon Monoxide. *Antioxid Redox Signal 4, 321-329*

Choi, C. H., Hiromura, M., and Usheva, A. (2003) — Transcription Factor IIB Acetylates Itself to Regulate Transcription. *Nature 424, 965-969*

Choi, C. H., Moser, J., Sobourin, N., Blagoev, K., Naughton, M., and Usheva, A. (2003) — YY1-DNA Interaction Results in a Significant Change of Electronic Context as Measured by Capacitance. *Biophys Chem 103, 109-115*

Hiromura, M., Choi, C. H., Sabourin, N. A., Jones, H., Bachvarov, D., and Usheva, A. (2003) YY1 is Regulated by O-linked N-acetylglucosaminylation (O-glcNAcylation). *J Biol Chem 278, 14046-14052*

Moser, J., Panepucci, R., Huang, Z. P., Li, W. Z., Z.F., R., Usheva, A., and Naughton, M. J. (2003) — Individual Free-Standing Carbon Nanofibers Addressable on the 50 nm Scale. *Journal of Vacuum Science & Technology B 21, 1004-1007*

Ohiro, Y., Usheva, A., Kobayashi, S., Duffy, S. L., Nantz, R., Gius, D., and Horikoshi, N. (2003) — Inhibition of Stress-Inducible Kinase Pathways by Tumorigenic Mutant p53. *Mol Cell Biol 23, 322-334*

Otterbein, L. E., Zuckerbraun, B. S., Haga, M., Liu, F., Song, R., Usheva, A., Stachulak, C., Bodyak, N., Smith, R. N., Csizmadia, E., et al. (2003) — Carbon Monoxide Suppresses Arteriosclerotic Lesions Associated With Chronic Graft Rejection and with Balloon Injury. *Nat Med 9, 183-190.*

Choi, C. H., Burton, Z. F., and Usheva, A. (2004) — Auto-Acetylation of Transcription Factors as a Control Mechanism in Gene Expression. *Cell Cycle 3, 114-115*

Choi, C. H., Kalosakas, G., Rasmussen, K. O., Hiromura, M., Bishop, A. R., Usheva, A. (2004) — DNA Dynamically Determines its Own Transcription Initiation. *Nucleic Acids Res 32, 1584-1590*

Yamashita, K., McDaid, J., Ollinger, R., Tsui, T. Y., Berberat, P. O., Usheva, A., Csizmadia, E., Smith, R. N., Soares, M. P., and Bach, F. H. (2004)—Biliverdin, a Natural Product of Heme Catabolism, Induces Tolerance to Cardiac Allografts. *FASEB J, in press*

Sarady, J. K., Zuckerbraun, B.S., Bilban, M., Wagner, O., Usheva, A., Liu, F., Ifedigbo, E., Zamora, R., Choi, A. M., Otterbein, L. E. (2004) — Carbon Monoxide Protection Against Endotoxic Shock Involves Reciprocal Effects on iNOS in the Lung and Liver. *FASEB J, in press*

Choi, C. H., Sabourin, N. A., Reagor, D. W., Redondo, A., Usheva, A. (2004) — Capacitance-Derived Dielectric Constants Demonstrate Differential Preinitiation Complexes in TBP-Independent and TBP-Dependent Transcription. *Biophys Chem, in press*

Research Support – Active Funding

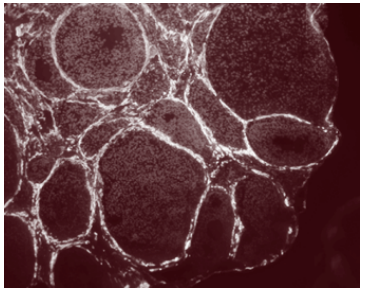
YY1 functions in vascular smooth muscle cells — Examination of multiple roles of YY1 in gene regulation in vascular smooth muscle cells and atherosclerosis *National Heart, Lung and Blood Institute HL62458-01A1 (PI: Anny Usheva-Simidjiyska) 06/2000-05/2005 NIH R01*

Physical principles, that determine the DNA features in gene transcription
Department of Energy and Los Alamos National LAboratory, DOE-47206
(Co-PI: Anny Usheva-Simidjiyska) 10/2003-09/2006

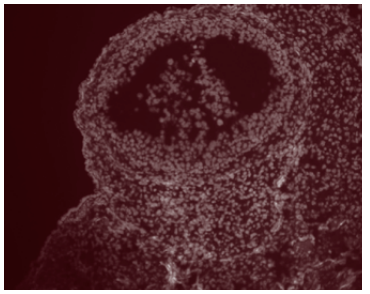
Cell cycle signaling and transcription factors in the vascular response to injury — MAP kinases-retinoblastoma protein-transcription factor YY1 interactions in vascular injury
Research grant—Mallinckrodt, Jr. Foundation (PI: Anny Usheva-Simidjiyska) 06/1999-06/2003

YY1 regulated transcription in human coronary artery smooth muscle cells during transition from arrest to active cell cycling — Characterization of YY1-dependent gene regulation in human coronary artery smooth muscle cells and its relationship to the cell cycle and atherosclerosis. *Young Scientist Development Grant—American Heart Association 9930081N (PI: Anny Usheva-Simidjiyska) 6/2000-12/2004*

Fluorescent microscopy of smooth muscle alpha actin expression and distribution in mouse ovaries



Young ovary



Ovary from 8 m old retired breeder. Nuclear staining was performed with hoehst. Smooth musde alpha actin was stained with FITC- conjugated primary anti - alpha actin antibody. Cryosections were prepared from frozen mouse ovary

Geoffrey Wong, M.D.

Dr. Geoffrey Wong, is involved with Dr. Oliver Kocher of the department of hematology in a research project funded by the Abbott Laboratories. The project looked at the impact of hypercoagulation gene mutations on pregnancy. Five thousand pregnant women from BIDMC were recruited for the study. The prevalence of the gene mutations was measured from this large population, and the impact of the gene mutations on pregnancy course, pregnancy outcome, maternal, fetal and neonate morbidities were outcome parameters measured.

Through the generous gift of a patient, Dr. Wong is able to concentrate his time on clinical research. He is embarking on a clinical study with Dr. Bruce Cohen of the division of maternal-fetal medicine to study triplet pregnancies delivered at BIDMC. He is also working on area of interest of prenatal ultrasound diagnosis with Dr. Deborah Levine of radiology.

David Ryley, M.D., Reproductive Endocrinology Fellow

The IVF low responder: do not rush to cancel — Dr. David A. Ryley, Beth Israel Deaconess Medical Center and Boston IVF, Boston, MA; Meredith Regan, Christine Connolly, Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, MA; Doria Harris, Boston IVF, Waltham, MA; Sigal Klipstein, Richard H. Reindollar, Beth Israel Deaconess Medical Center and Boston IVF, Boston, MA.

This study represents the largest series of data on outcomes (i.e. delivery rates) of infertility patients with a poor response to controlled ovarian hyperstimulation. We found that reasonable delivery rates (12.2-30.3%) were obtained in patients with 4 or less ovarian follicles resulting from ovarian hyperstimulation up to the age of 41 years. A logistic regression analysis was used to provide a table of these delivery rates. This data can be used by the clinician during the counseling of patients on whether or not they should continue an IVF treatment cycle.

The IVF Poor Responder: Predicting a Good Outcome — David A. Ryley, Beth Israel Deaconess Medical Center and Boston IVF, Boston, MA; Meredith Regan, Christine Connolly, Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, MA; Doria Harris, Boston IVF, Waltham, MA; Lorna S. Timmreck, Richard H. Reindollar, Beth Israel Deaconess Medical Center and Boston IVF, Boston, MA.

This study provides the largest series of data on delivery rates of patients who are defined as poor responders to ovarian hyperstimulation based on peak serum estradiol levels 5 00 pg/ml, follicle counts 4 , or both. Reasonable delivery rates were found up to the age of 43 years in patients with a normal follicular response, but a low peak serum estradiol level. Reasonable delivery rates were also noted in patients up to the age of 41 years with a low follicle count but a normal peak serum estradiol level. And, in patients with both a low peak serum estradiol level and a low follicle count, pregnancy rates were all above 10% up to the age of 38 years. A logistic regression analysis was done so as to provide a table of delivery rates. This data will assist the clinician in his or her counseling of poor responder couples. Many cycles defined by these parameters would have been cancelled due to a presumed poor delivery rate. This data challenges that approach to the treatment of “poor responders”.

Characterization of the Human FORMIN2 Gene — This research expands on the work of Drs. Benjamin Leader and Dr. Phillip Leder at HMS. They described the mouse formin2 gene, and published their results in Nature in November, 2002. Mutations in the mouse gene resulted in hypofertility, due to oocyte

maturation arrest. formin2 -/- oocytes are unable to correctly position the meiotic spindle during Meiosis I, and therefore have a retained polar body and aberrant development. In our study, we were able to map the complete cDNA sequence of the human FMN2 gene, and design PCR primer sets to amplify the exons in patients with normal fertility. We hope to use this data to compare the FORMIN2 gene in patients with normal and unexplained infertility due to oocyte maturation arrest. (See #4).

The Influence of Body Mass Index on the Outcome of 6,827 IVF Cycles
This research describes the influence of BMI on pregnancy and implantation rates in patients undergoing IVF. Patients were categorized according to 5 BMI categories, correlating with weight classification by BMI as determined by the National Heart, Lung, and Blood Institute as well as the World Health Organization. The goal of this research is to determine the effect, if any, of extremes of BMI on IVF success. Previous retrospective and prospective data have demonstrated conflicting results, and we hope that our large IVF database will further define the relationship between BMI and IVF pregnancy rates. Our research is to be presented at the Annual Meeting of the American Society of Reproductive Medicine in Philadelphia in October, 2004.

Peer-Reviewed Publications

Ryley DA, Moorman DW, Hecht JL, Alper MM — A Mesothelial Cyst of the Round Ligament Presenting as an Inguinal Hernia Following Gonadotropin Stimulation During In Vitro Fertilization. *Feril. Steril. (in press)*

Ryley DA, Berger MJ, Regan M, Harris D, Klipstein S, Reindollar RH — Outcomes of 6,462 IVF Cycles With a Low Peak Serum Estradiol and/or Low Number of Mature Follides Resulting From Controlled Ovarian Hyperstimulation: a 7-year review*(submitted)*

Ryley DA, Berger MJ, Regan M, Harris D, Timmreck L, Reindollar RH — The IVF Low Responder: Outcome Differences Based on 1-2, 3, and 4 Mature Follicles: a 7-year Retrospective Analysis" *(submitted)*

Ryley DA, Wu HH, Leader B, Zimon A, Reindollar RH, Gray MR — Characterization of the Human FORMIN2 (FMN2) Gene and Analysis of FMN2 Gene Mutations in Patients With Unexplained Infertility*(submitted)*

Klipstein S, Regan M, Ryley DA, Goldman M, Alper MM — A Last Chance for Pregnancy Associated With Advanced Maternal Age. A Review of 2,705 IVF Cycles Initiated in Women Aged Forty and Above. *(submitted)*

Peters M, Ryley DA, Lockwood C — Hereditary Angioedema and Immunoglobulin a Deficiency in Pregnancy. *Obstet. Gynecol. 1988; 72: 454*

Book Chapters

Timmreck LS, Ryley DA, Reindollar RH. — Disorders of Sexual Development. *In: Carr, Blackwell, Azziz, editors. Essentials in Reproductive Medicine. New York: McGraw-Hill (in press)*

Abstracts

Ryley DA, Bayer SR, Eaton J, Zimon AE, Klipstein S, Reindollar RH — Influence of Body Mass Index (BMI) on the Outcome of 6,827 IVF Cycles. *To be Presented at the American Society for Reproductive Medicine Annual Meeting, Philadelphia, PA, 2004. Oral Presentation*

Ryley DA, Wu HH, Zimon AE, Reindollar RH, Gray MR — Characterization of the Human FORMIN2 (FMN2) Gene and Analysis of the FMN2 Gene in Patients with Unexplained Infertility. *The Society for Gynecologic Investigation Annual Meeting, Houston, TX, 2004. J. Soc. Gynecol. Inves. 2004; 11(2) Suppl: 132A*

Yang LC, Timmreck LT, Galper S, Ryley DA, Klipstein S, Reindollar RH—Gonadotropin / IUI in Women 40 Years and Older: Success Rates from 263 cycles. *The Annual Assembly of the New England Fertility Society: Practice and Science, Bretton Woods, New Hampshire, 2004*

Zimon AE, Oellinger R, Ryley DA, Reindollar RH, Usheva A. — Gene Expression Profiling of Young and Aged Mouse Ovaries. *The Society for Gynecologic Investigation Annual Meeting, Houston, TX, 2004. J. Soc. Gynecol. Inves. 2004; 11(2) Suppl: 281A*

Ryley DA, Regan M, Connolly C, Harris D, Klipstein S, Reindollar RH — The IVF Low Responder: Do Not Rush to Cancel. *The American Society for Reproductive Medicine Annual Meeting, San Antonio, TX, 2003. Fertil. Steril. 2003; 80(3) Suppl: 59-60. Oral Presentation*

Ryley DA, Regan M, Connolly C, Harris D, Timmreck L, Reindollar RH — The IVF Poor Responder: Predicting a Good Outcome. *The American Society for Reproductive Medicine Annual Meeting, San Antonio, TX, 2003. Fertil. Steril. 2003; 80(3) Suppl: 99. Oral Presentation*

Wu HH, Ryley DA, Leader B, Zimon A, Reindollar RH, Gray MR — Characterization of the Human FORMIN2 (FMN2) Gene. *The American Society for Reproductive Medicine Annual Meeting, San Antonio, TX, 2003. Fertil. Steril. 2003; 80(3) Suppl: 252-253*

Klipstein S, Eyvazzadeh A, Thornton KL, Timmreck LS, Ryley DA, Reindollar RH—High Order Multiple (HOM) Pregnancies and IVF Cycle Number: Is There an Association? *The American Society for Reproductive Medicine Annual Meeting, San Antonio, TX, 2003. Fertil Steril. 2003; 80(3) Suppl: 176*

Klipstein S, Harris DH, Alper MM, Ryley DA, Timmreck L, Reindollar RH — Success Rates in Women Undergoing In Vitro Fertilization (IVF) at Age 40 and Above at the Nation's Largest IVF Center. *The Society for Gynecologic Investigation Annual Meeting, Washington, DC, 2003. J. Soc. Gynecol. Inves. 2003; 10(2) Suppl: 286A*

Alison Zimon M.D.

Dr. Alison Zimon is a fellow and clinical instructor in reproductive endocrinology and infertility. She received her undergraduate degree at Harvard College and medical degree at Yale University School of Medicine. She completed her residency at Beth Israel Deaconess Medical Center. Presently a second year fellow, she is working under the mentorship of Dr. Richard Reindollar and Dr. Anny Usheva and pursuing her interest in the molecular basis of ovarian aging.

Research Activities

- Gene expression profiling of ovarian aging in the murine model
- Age-dependent gene expression profiles of luteinized granulosa cells of women undergoing infertility treatment

Funding Activity (2001 – present)

NIH Loan Repayment Program — Gene Expression Profiling of Ovarian Follicular Cells from Mice of Young and Old Reproductive Age, 2004-2005

Board of BIDMC Obstetrics & Gynecology Foundation — Gene Expression Profiling of Ovarian Aging in the Murine Model, 2004

Original Articles (2001 – present)

Karnis MF, Zimon AE, Lalwani SI, Timmreck LS, Klipstein S, Reindollar RH — The Risk of Death in Pregnancy Achieved through Oocyte Donation in Patients with Turner Syndrome: A National Survey. *Fertil Steril, 2003: 80(3): 498-501*

Abstracts (2001 – present)

Zimon A, Witmyer J, Reindollar R. Blastocyst versus day-3 embryo transfers — A Comparison of Fresh and Thaw Cycle Cumulative Outcomes. *Fertil Steril 2002; 76(3S): S138*

Wu HH, Ryley DA, Leader B, Zimon A, Reindollar RH, Gray MR — Characterization of the Human FORMIN2 (FMN2) Gene. *Fertil Steril 2003; 80(3S): S252*

Zimon AE, Ollinger R, Ryley DA, Reindollar RH, Usheva A — Gene Expression Profiling of Young and Aged Mouse Ovaries. *J Soc Gynecol Investig 2004; 11(2S): 281A*

Zimon A, Erat A, Bissell B, Ryley D, Koulova A, Reindollar RH, Usheva A — NF-KB Dependent Stress Response Pathways are Involved in Ovarian Aging. *XVth Ovarian Workshop, Vancouver, BC July 29-31, 2004*

Research Projects

Lamellar Body Numerical Density Project 6/2001-6/2002 — Study performed to compare the reliability of the amniotic fluid lamellar body numerical density (LBND) assay with lecithin / sphingomyelin ratio (L/S) assay and phosphatidy / glycerol (PG) assay in pregnancies complicated by maternal diabetes mellitus (DM). To determine an LBND value that maximizes sensitivity and specificity in predicting fetal lung maturity.

Sexual Assault Study 6/2002- 6/2003 — Analysis of 649 Cases of Sexual Assault To describe the Epidemiology of sexual assault at a large academic center in Canada and to compare this group with sexual assault victims in other countries. The purpose of our study was to describe the victim, assailant, type of assault and to provide descriptive data.

Relaxation Techniques During Mammography 8/2002 to Present — The purpose of this study was to determine if listening to a relaxation audio tape during mammograms decreases subjective reports of pain and anxiety and increased compliance with screening guidelines.

High Order Multiple (HOM) Pregnancies and IVF Cycle Number: 10/03 to present —This analysis was undertaken to determine factors placing women at risk for conceiving HOMs. We hypothesized that triplets may result from more aggressive treatment in couples who fail to conceive in early cycles, perhaps resulting from the transfer of more embryos.

MR evaluation of suspected acute appendicitis in pregnancy 6/2002 to Present—This project was undertaken to evaluate the diagnostic value of MR imaging in pregnant patients with clinical suspicion of acute appendicitis.

Patient age and physician embryo transfer rates within an In Vitro Fertilization Program May 2004 — The present analysis was undertaken to determine whether such variations among physician transfer rates persist for patients over the age of forty years, a subgroup known to have lower pregnancy rates from IVF.

Publications

Sigal Klipstein, Aimee Eyvazzadeh, Kim L. Thornton, Lorna S. Timmreck, David A. Ryley and Richard H. Reindollar — High Order Multiple (HOM) Pregnancies and IVF Cycle Number: is There an Association? *Fertility and Sterility, Volume 80, Supplement 3, September 2003, Page 176*

Sigal Klipstein, Aimee Eyvazzadeh, Kim L. Thornton, Lorna S. Timmreck, David A. Ryley, Richard H. Reindollar — High Order Multiple (HOM) Pregnancies and IVF Cycle Number: Is There an Association? *Poster presentation at the 59th Annual Meeting of the American Society for Reproductive Medicine held October 11-15, 2003, in San Antonio, Texas.*

Aimee Eyvazzadeh, Ivan Pedrosa, Eric Chiang, Jodi Abbott, Neil M. Rofsky, Deborah Levine. MR — Evaluation of Suspected Acute Appendicitis in Pregnancy. *Accepted for Poster Presentation at Society for Maternal Fetal Medicine Meeting February 2004.*

Alice D. Domar, Aimee Eyvazzadeh, Sarah Allen, Kara Roman, John Orav, Nile Albright, Janet Baum, M.D. — Relaxation Techniques Do Not Decrease Anxiety and Pain During Mammography. *Abstract accepted for presentation at RSNA 11/03.*

Alice D. Domar, Aimee Eyvazzadeh, Sarah Allen, Kara Roman, John Orav, Nile Albright, Janet Baum, M.D. — Relaxation Techniques Do Not Decrease Anxiety and Pain During Mammography. *American Journal of Roentgenology. April 2004*

Pedrosa, AD Eyvazzadeh, B Siewert, D Levine, NM Rofsky — MRI Evaluation of Suspected Acute Appendicitis in Pregnancy. Accepted for Presentation at American Roentgenology Radiology Society May 2004. *Scientific Program*

Aimee Eyvazzadeh, Ivan Pedrosa, Neil M. Rofsky, Bettina Siewert, Norman Farrar, Jodi Abbott, Deborah Levine — MR Imaging of Right-Sided Abdominal Pain in Pregnancy. *American Journal of Roentgenology. January 2004*

Eyvazzadeh A, Pedrosa I, Rofsky NM, et al — Pictorial essay. MRI of Right-Sided Abdominal Pain in Pregnancy. *Pictorial essay, coming out next month.*

David Ryley, Aimee Eyvazzadeh, Richard Reindollar — DVD Visual Tutorial and Teaching Guide for the Harvard Medical School Course IN708.0g: Human Systems Module II, Part 3, Disorders of the Reproductive Systems

A.Eyvazzadeh, S. Ghadir, A. DeCherney — Fifth World Congress on Controversies in Obstetrics and Gynecology and Infertility, Management of Intramural Fibroids in Infertility. *Published in Scientific Program. June 2004*

A. Eyvazzadeh, D. Ryley, A. Penzias, M. Alper, R. H. Reindollar; Beth Israel Deaconess Medical Center, Boston, MA, Beth Israel Deaconess Medical Center and Boston IVF, Boston, MA— Does Patient Age Impact Physician Embryo Transfer Rates Within an In Vi t ro Fertilization Program? *Presented at ASRM October 2004.*

A. Eyvazzadeh — The Question *UCLA Beat, UCLA School of Medicine Literary journal, May 2001, Volume III, Page 37*

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