

Summer 2008



Advancing Ob/Gyn

Developments from Yale Obstetrics,
Gynecology & Reproductive Sciences

Message from the Chair

**Greetings from Charles J. Lockwood, MD, The Anita O'Keefe
Young Professor of Women's Health and Chair**

It gives me great pleasure to share with you this latest issue of *Advancing Ob/Gyn*. Within these pages we summarize only a few of the recent clinical developments and new initiatives at Yale Obstetrics, Gynecology & Reproductive Sciences. While we have many recent developments in our three mission areas of education, clinical care, and research, we have selected topics that we believe will be of most interest to you as a medical professional.

As in past issues, our focus is on topics of a controversial nature, as well as on new treatment or screening modalities developed here at Yale. Many of the topics you will find within these pages can have an immediate impact on your practice.

We hope that our newsletter will serve as a valuable source of contemporary thinking on these topics for ob/gyns, internists, midwives, fellows, and residents. As always, we welcome your comments and suggestions.

Charles J. Lockwood, MD

Yale Obstetrics and Gynecology
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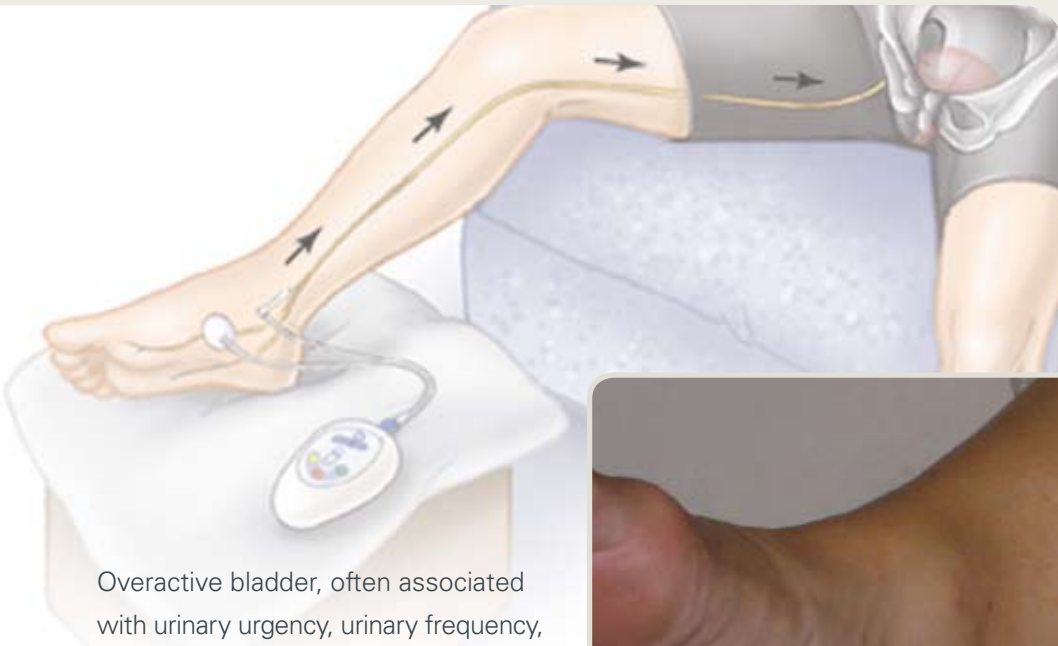


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And the Ankle Bone's Connected to the ... Bladder? Richard Bercik, MD



Overactive bladder, often associated with urinary urgency, urinary frequency, nocturia, and urinary incontinence, can be very disturbing and distressing to patients. Conventional therapies, which include anticholinergic medication, biofeedback, implantable (central) neurostimulation, and behavioral therapy, have limitations. Side effects frequently limit the efficacy of anticholinergic medication, while the insertion of a vaginal probe for biofeedback often makes this treatment uncomfortable. Many patients are unwilling to undergo the two surgical procedures required for implanting a central nervous system neurostimulator.

Percutaneous Tibial Nerve Stimulation (PTNS) is an office-based procedure that has proven to help many patients with overactive bladder. A needle is inserted behind the ankle, above the medial malleolus into the posterior tibial nerve, followed by the application of electrical stimulation. Because common nerve roots are shared by the posterior tibial nerve and the

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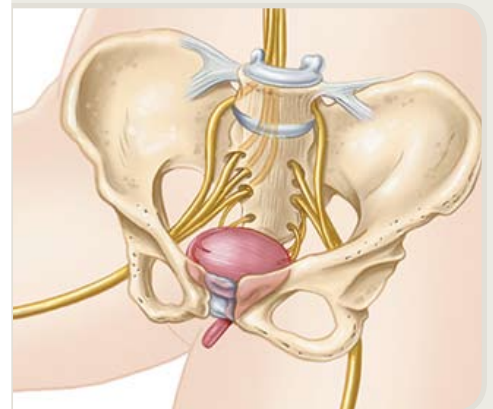


bladder, stimulation of this nerve has been shown to improve voiding function and reduce urgency and urge incontinence. PTNS treatment usually involves weekly 30-minute sessions for 10 to 12 weeks.

The Division of Urogynecology and Reproductive Pelvic Surgery has been using PTNS for approximately one year for patients with urinary urgency, urinary frequency, and urge incontinence. Generally, patients who choose not to take medication, who have not responded to medication, or in whom medication is contraindicated have been offered this therapy. Approximately 80% of treated patients have responded with

improvement in symptoms and have been happy with the results.

For a more detailed discussion of this topic, as well as an author bio, please visit www.yaleobgyn.org/advancing.



Society for Gynecologic Oncologists “Fight Night”

Peter Schwartz, MD

Conventional Radical Surgery vs. Neoadjuvant Chemotherapy as the First Step in the Management of Epithelial Ovarian Cancer

Conventional treatment of advanced stage epithelial ovarian cancer involves initial surgical removal of virtually all visible cancer, followed by platinum-based combination chemotherapy. On March 10, 2008, Dr. Peter Schwartz debated Dr. Dennis Chi at the first Society of Gynecologic Oncologists “Fight Night” at the Annual Meeting of the Society of Gynecologic Oncologists in Tampa, Florida. Dr. Chi, a gynecologic oncologist practicing at Memorial-Sloan Kettering Cancer Center (MSKCC), held that aggressive cytoreduction should be the first step in treatment. Dr. Schwartz advocated neoadjuvant chemotherapy for advanced stage disease, an approach used at Yale in selected patients since 1979.

Dr. Chi cited reports from MSKCC showing that the first step in managing ovarian cancer should be aggressive cytoreductive surgery. He emphasized that he was able to “optimally cytoreduce” residual disease in 70% of his patients.

Dr. Schwartz countered that current ovarian cancer treatment is no different than it was in 1974 when Griffiths reported that patients with no residual disease following surgery had a mean survival of 39 months.

Dr. Schwartz challenged Dr. Chi on his data as only 22% of the patients who Dr. Chi operated on for advanced stage ovarian cancer had no visible residual disease. Dr. Schwartz then presented Yale data in which patients with advanced stage ovarian cancer who received neoadjuvant chemotherapy followed by aggressive cytoreductive surgery had the same survival for Stage III disease as patients who underwent aggressive cytoreductive surgery first. Additionally, patients who underwent surgical cytoreduction following neoadjuvant chemotherapy felt better prepared for the surgery and the surgery was statistically shorter, and associated with significantly less blood loss, shorter SICU stays and shorter hospitalizations compared to conventionally treated patients.



Photo Credit: Nationwide Photographers, Martin Allred

Using an electronic voting system, the audience of approximately 1000 people voted the debate in favor of Dr. Schwartz. Dr. Schwartz has been given a championship belt for winning the “fight” and is now referred to by colleagues as “champ.”

For a more detailed discussion of this topic, as well as an author bio, please visit www.yaleobgyn.org/advancing.



Pediatric and Adolescent Gynecology

Beth Rackow, MD

The American College of Obstetricians and Gynecologists recommends that a young woman's first visit with an obstetrician-gynecologist occur between the ages of 13 and 15.

This visit allows time to establish a relationship and discuss issues of a confidential nature. Important topics to review include normal pubertal development and menstruation, healthy eating habits and body image, safety, and prevention of pregnancy and sexually transmitted diseases.

It is also an ideal time to discuss preventive health care, including availability of the quadrivalent human papillomavirus vaccine, approved for administration to females aged 9 – 26 years. Although maximally effective if received prior to HPV exposure, it is also beneficial for already sexually active females.

Regardless of vaccination status, cervical cytology screening recommendations are unchanged: cervical cancer screening is not indicated until a young woman has been sexually active for three years or reaches age 21.

Routine preventive health care may identify gynecologic problems in infants, children, and adolescents that are often quite different from those affecting adult women. Common gynecologic disorders in these age groups include vaginal discharge, menstrual

disorders, pelvic pain, congenital anomalies of the reproductive tract, abnormal puberty and amenorrhea.

For a more detailed discussion of this topic, as well as an author bio, please visit www.yaleobgyn.org/advancing.



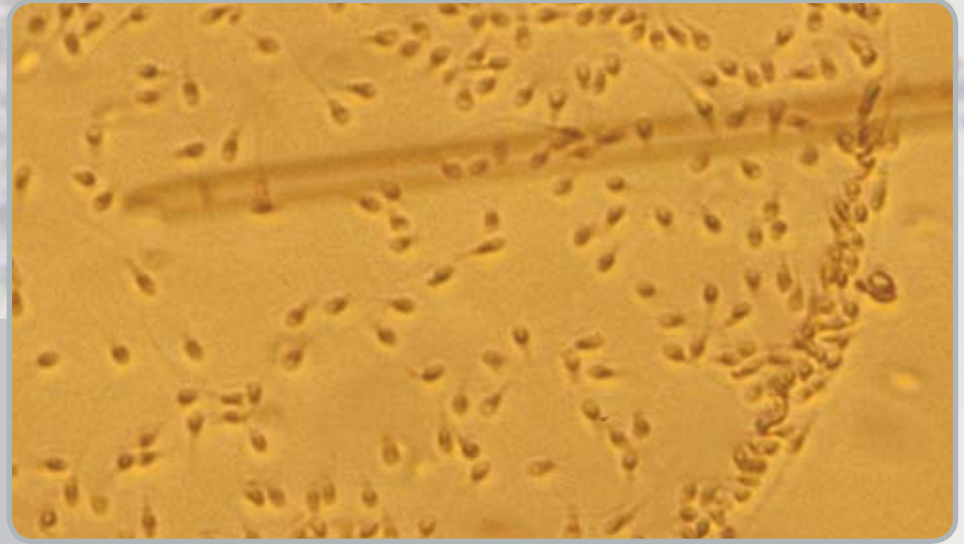
Sperm-Hyaluronic Acid Interaction: Assessment of Male Fertility and Selection of Mature Sperm for ICSI

Gabor Huszar, MD

Research conducted at the Yale Sperm Physiology Laboratory has led to a breakthrough in selecting mature sperm for use in *in vitro* fertilization treatment.

The hyaluronic acid (HA) receptor of mature sperm, coupled with an HA-coated sperm selection Petri dish, allows direct observation of sperm-HA binding and ICSI selection of single mature sperm. HA-binding identifies sperm that would have been selected by the zona pellucida in natural and IVF fertilization. Conversely, sperm with arrested maturity do not bind to either hyaluronic acid or to the zona pellucida.

Immature spermatozoa, present in every ejaculate, are characterized by attributes of arrested sperm maturity, including cytoplasmic retention, persistent histones, and DNA chain breaks. The frequencies of sperm with chromosomal disomy and diploidy are reduced by four-to-five-fold in HA-bound sperm versus the unselected sperm fraction of the same semen sample. This is one of the great advantages of using HA-mediated ICSI sperm selection. Combined studies of sperm shape and chromosome probes have demonstrated that morphology does not distinguish haploid (normal) and aneuploid sperm; the best-looking sperm are not always mature or of high genetic integrity.



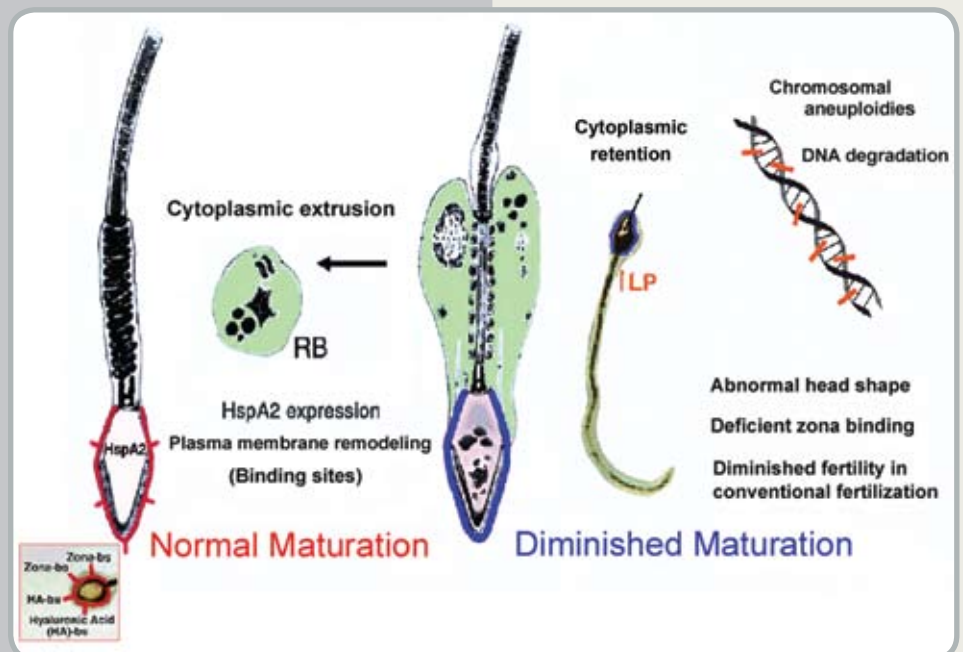
Hyaluronic acid-bound sperm ready for selection for ICSI procedure.

HA-binding mediated sperm selection was developed at Yale in our Sperm Physiology Laboratory, directed by Gabor Huszar, MD.

The HA-sperm interaction method provides an improved approach for semen analysis, while HA-mediated ICSI sperm selection mitigates genetic concerns related to ICSI,

addressing a potential major public health concern. HA-mediated ICSI sperm selection and the sperm HA-binding male fertility test have been approved by the FDA and the European regulatory authorities.

For a more detailed discussion of this topic, as well as an author bio, please visit www.yaleobgyn.org/advancing.





Patient Safety in Obstetrics

Edmund F. Funai, MD

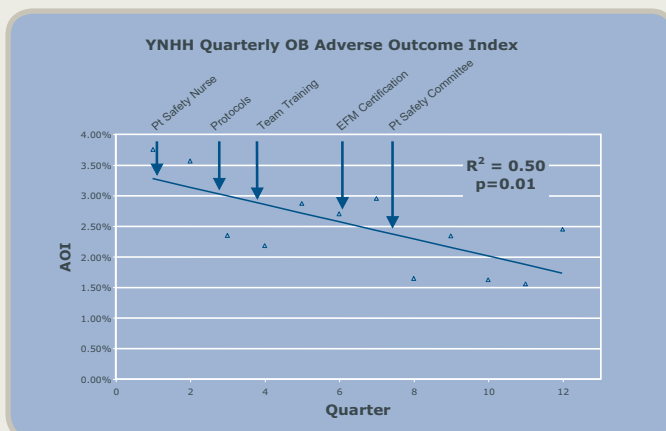
To improve communication, and to enhance overall safety, Yale's Obstetric service has embarked on a broad series of initiatives. Every member of the team has had formal training in communication based upon the principles of Crew Resource Management (CRM) developed by the aviation industry. In our version of CRM, we have two teams on Labor and Delivery. The core team consists of the primary caregiver (obstetrician, resident or midwife, or all three) and the primary nurse. A combined coordinating and contingency team backs up the core team. The Yale Maternal-Fetal Medicine hospitalist and charge nurse coordinate patient flow, triage patients in the queue for Cesarean deliveries, adjudicate competing claims for induction slots, and round with the core teams to ensure that all appropriate information is available and has been considered.

Beyond CRM, we have implemented a series of safety enhancements: 1) creation of a full-time Patient Safety nurse

to support performance improvement, 2) protocol-based standardization of common procedures such as administration of oxytocin, 3) adoption of standardized terminology for interpretation of fetal heart rate monitoring, culminating in a national certification exam, 4) multidisciplinary oversight of performance by a department-based Patient Safety Committee, and 5) simulation and drills for high risk/low frequency events.

Over approximately three years, we have seen more than a 50% reduction in adverse events, while staff perception of the overall safety climate improved 30%.

For a more detailed discussion of this topic, as well as an author bio, please visit www.yaleobgyn.org/advancing.



Adverse events have declined significantly since introduction of our Patient Safety Initiative.

In Memoriam: Harold Berhman

With great sadness we share the passing of Harold R. Behrman, PhD, Professor of Obstetrics, Gynecology & Reproductive Sciences, and of Pharmacology. Dr. Behrman served for over 30 years on the Yale faculty and had a profound impact on this community. His research and mentoring greatly impacted the field of reproductive biology. We will sorely miss Hal.

To continue his legacy, the Department of Obstetrics, Gynecology & Reproductive Sciences will establish the Dr. Harold R. Behrman Memorial Lectureship to support the department's ongoing effort to bring world-renowned researchers and clinical leaders to our community and recognize Dr. Behrman's lasting impact on his field as well as on students, fellows and faculty.

Below are giving details for those of you who wish to contribute to the Lectureship fund.

Giving Information

Attn: Chip Edmonds
Development Office
Yale School of Medicine
Box 7611
New Haven, CT 06519-0611
Checks can be made payable to:
Yale School of Medicine
Memo line: Dr. Harold R. Behrman
Memorial Lectureship

Featured Physician: Lubna Pal

Dr. Lubna Pal is Director of the Reproductive Aging and Bone Health Program at Yale Reproductive Endocrinology, specializing in the areas of infertility, reproductive aging and menopause, low bone mineral density, and reproductive endocrinology. She is Board Certified in both Obstetrics & Gynecology and Reproductive Endocrinology & Infertility and is certified by the International Society for Clinical Densitometry for interpretation of bone mineral density studies. Her clinical interests are reproductive endocrinopathies including polycystic ovarian syndrome (PCOS), central reproductive disturbances attributable to hypothalamic and pituitary disorders, and obesity-related reproductive dysfunction.



Declining Ovarian Reserve... A Critical Determinant of Reproductive Health

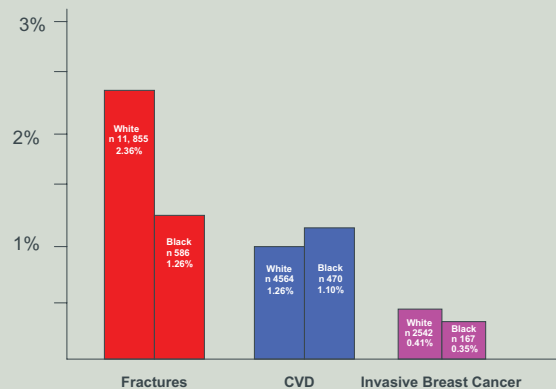
Osteoporotic fractures and cardiovascular disease (CVD) in women are associated with the postmenopausal period. A growing body of evidence suggests that estrogen therapy confers protection against initiation of processes that underlie these two diseases. While the skeletal benefits of estrogen are well recognized across all ages in women, there is mounting evidence that,

if commenced prior to initiation of atherosclerosis, estrogen therapy also confers cardio-protection in menopausal women.

The term “ovarian reserve” is a quantitative estimate of ovarian function. Declining ovarian reserve prior to menopause reflects the early loss of ovarian hormone production and identifies reproductive aging. The hormonal profile of decreased ovarian reserve in young women shares features with the profiles of older perimenopausal women, which may be of significance in the initiation of processes that underlie skeletal loss and CVD. It is crucial to appreciate the importance of timing in beginning preventive care concomitant with a decline in ovarian physiology, years prior to the final menstrual period.

For a more detailed discussion of this topic, please visit www.yaleobgyn.org/advancing.

Annualized Age Adjusted Disease Rates (%) in Postmenopausal Women (n=83,724) Enrolled in Observational Arm of WHI by Race over 7.7 ± 2.6 Years



Cauley JA et al. Osteoporosis International, 2008.

The bulk of health care burden in an aging female population is attributable to two preventable entities: cardiovascular disease and osteoporosis. Somber Facts: Eight million US women suffer from osteoporosis; projected figure for 2020 is 10 million. Four in 10 white and two in 10 black US women over age 50 will experience osteoporotic fracture in their lifetimes (NOF 2002). Almost 39 percent of all female deaths in America occur from CVD. In 2003, 483,842 women died of CVD (AHA 2003).

Community Doctors and Midwives Support Yale Ob/Gyn Mission

Thanks in large part to the teaching services of our community-based ob/gyns and midwives, our residency program was recently re-approved for another four years. Over the past year, their dedication to our educational mission has enabled us to:

- Continue to increase annual vaginal deliveries per graduating resident, with this year's graduating chiefs surpassing the national average for vaginal deliveries.
- Complete the 67th certified year of our highly acclaimed residency training program.
- Offer many valuable lectures on clinical topics in Ob/Gyn.

We are grateful for the time and effort invested by our colleagues in fulfilling our educational training mission, and we thank them for continuing to include residents as participants in their vaginal deliveries.

Congratulations to the following faculty who received awards for their commitment to residency education at our annual C. Lee Buxton Residents' Research Day ceremony held May 30 in New Haven, CT:

Howard Simon, MD – Temple Surgical Award – Awarded to the physician who has demonstrated superior teaching skills in surgical techniques.

Eliza Holland, CNM – Midwifery Award – For special efforts in training residents and medical students.

Stephen Thung, MD – The 3rd Lee Buxton Faculty Teaching Award for Resident Education – For recognition of faculty commitment to the education of residents.

Brian Karsif, MD – The 3rd Lee Buxton Faculty Teaching Award for Medical Student Education – For recognition of faculty commitment to the education of medical students.

Beth Rackow, MD – APGO Medical Foundation Award – For excellent teaching by a faculty member, selected by the medical students.

Mert Bahtiyar, MD – CREOG National Faculty Award – For promoting high standards of residency education in the field of Obstetrics & Gynecology.

Seth Guller, PhD – The Harold Behrman Award – In recognition of the scientist who demonstrates a deep commitment to mentoring students, residents and fellows.

David Lima, MD – Stanley Laviertes Award – Presented to the community physician voted by the Yale Obstetrics and Gynecology residents as representing an outstanding example of superb patient care, devotion to resident teaching, and overall clinical excellence.

On the front cover: The newest member of our gynecologic oncology faculty, Dr. Alessandro Santin, at work in his laboratory.

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