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Henry Ford Health System Publication List April 2009

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You can access this page at http://www.henryfordconnect.com/sladen.cfm?id=436.

Anesthesiology
Nagaraja, T. N., K. Karki, J. R. Ewing, J. D. Fenstermacher and R. A. Knight (2009). "Enhanced Spatial Resolution of Stroke-induced Acute Blood-Brain Barrier Damage by a Combination of Step-down Infusion of a Magnetic Resonance Contrast Agent and Quantitative Patlak Permeability Maps." Stroke **40**(4): E139-E140. **Article Request Form** *Sladen Library has an electronic subscription, but the issue for this article was not available online at the time of this publication.*

Henry Ford Health System, Detroit, MI USA.
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Behavioral Services
Coffey, E. and K. K. Patra (2008). Cambridge Textbook of Effective Treatments in Psychiatry. P. Tyrer and K. R. Silk. Cambridge, U.K., Cambridge University Press. WM 400 C178 2008

Henry Ford Health System, Detroit, MI.
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Behavioral Services
Eshelman, A. K., S. Mason, H. Nemeh and C. Williams (2009). "LVAD destination therapy: applying what we know about psychiatric evaluation and management from cardiac failure and transplant." Heart Fail Rev **14**(1): 21-8. **PDF Full-Text**

BioScience, Henry Ford Hospital/CFP6, 2799 West Grand Boulevard, Detroit, MI 48202, USA. aeshelm1@hfhs.org

Left ventricular assist devices (LVADs) have evolved into long-term use as destination therapy for those with severe end-stage heart failure due to other medical risks. Success with LVAD depends on adherence to a complicated mechanical regimen, and acceptance of a life that is far from normal. Patients with LVADs share characteristics with other end-stage cardiac failure patients and those waiting for or receiving heart transplants. Understanding the more thoroughly studied issues of psychiatric disorders, adherence, and behavioral correlates of success in heart failure and transplantation may identify feasible strategies for optimizing care of LVAD patients and suggest directions for future research. Depression and distress complicate post-transplant care. Psychiatric morbidity

is associated with poor outcomes, including graft rejection, non-adherence, hospitalizations, infection, and death. With a high risk of embolic neurological events, patients' ability for self-care may be compromised. Psychiatric symptoms are underdiagnosed and undertreated, which may impact overall survival and quality of life.

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Behavioral Services

Ketterer, M. W. and W. Knysz (2009). "Screening, diagnosis & monitoring of depression/distress in CHF patients." Heart Fail Rev **14**(1): 1-5. **PDF Full-Text**

Henry Ford Hospital/CFP6, 2799 West Grand Boulevard, Detroit, MI 48202, USA. MKetter1@hfhs.org

Objective and validated measures of depression/distress (anxiety and anger) are available and readily usable at the bedside or in clinic. Foremost among these is the Patient's Health Questionnaire--an adaptation of DSM IV criteria for Major Depressive Disorder that permits administration and scoring by nursing or physician personnel, and quantification of the intensity of depression. A score of 10 or greater indicates a need for evaluation/treatment. Because of patient denial/minimization/alexithymia, PHQ negatives should undergo further screening by having a spouse or friend complete a depression/distress rating scale. The only standardized, normed, and validated spouse/friend scale presently available is the Ketterer Stress Symptom Frequency Checklist, which is available by internet.

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Behavioral Services

Parvizi, J., K. L. Coburn, S. D. Shillcutt, C. E. Coffey, E. C. Lauterbach and M. F. Mendez (2009). "Neuroanatomy of Pathological Laughing and Crying: A Report of the American Neuropsychiatric Association Committee on Research." Journal of Neuropsychiatry and Clinical Neurosciences **21**(1): 75-87. **PDF Full-Text**

Stanford Univ, Dept Neurol, Sch Med, Stanford, CA 94305 USA. Mercer Univ, Sch Med, Dept Psychiat, Macon, GA 31207 USA. Henry Ford Hlth Syst, Dept Psychiat, Detroit, MI USA. Univ Calif Los Angeles, Dept Neurol, Los Angeles, CA 90024 USA.

Pathological laughing and crying (PLC) is a clinical condition that occurs in patients with various neurological disorders. It is characterized by the presence of episodic and contextually inappropriate or merely exaggerated outbursts of laughter and/or crying without commensurate feelings. This review provides an in depth analysis of the neuroanatomy of lesions seen in patients with this clinical condition, discusses the relevant functional neuroimaging and electrophysiological stimulation studies in human subjects, and summarizes the current treatment options. It concludes with a presentation of the remaining questions and directions for future research.

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Biostatistics & Research Epidemiology

Chen, X. G. and K. J. Woodcroft (2009). "Polymorphisms in metabolic genes CYP1A1 and GSTM1 and changes in maternal smoking during pregnancy." Nicotine & Tobacco Research **11**(3): 225-233. **PDF Full-Text**

Wayne State Univ, Ann Adams Dept Pediat, Prevent Res Ctr, Detroit, MI 48201 USA. Henry Ford Health System, Dept Biostat & Res Epidemiol, Detroit, MI USA. jimchen@med.wayne.edu

Studies have documented the role of variations in genes that encode metabolic enzymes in altering the effects of maternal smoking on child health. We assessed the association of the MspI polymorphism in CYP1A1(*2A) and the null GSTM1 with maternal smoking behavior during pregnancy. Smoking data for women during pregnancy were derived through in-person interviews and from genotyping data from buccal cell DNA for 165 smoking mothers (85% Black) accompanying their children to Children's Hospital of Michigan in Detroit. The

number of daily smokers declined from 157 (95.2%) 30 days prior to pregnancy to 81 (49.1%) by the last trimester. The polymorphic variants of CYP1A1*2A (TC or CC) were positively associated with self-reduction and spontaneous quitting and negatively associated with persistent smoking. After allowing for the effect from covariates, we found the adjusted odds ratio (OR) for the association of any C allele to be 2.12 (95% CI = 1.00-4.61) for self-reduction, 1.71 (95% CI = 1.00-2.91) for ever quit smoking, and 0.53 (95% CI = 0.31-0.91) for persistent smoking. The null GSTM1 polymorphism was not associated with any of the three smoking measures. The single base substitution in the 3' noncoding region of the phase-1 metabolic gene CYP1A1 may facilitate self-reduction and quitting of tobacco smoking during pregnancy. This finding provides new data on the possible genetic etiology of maternal smoking during pregnancy and suggests the need to assess genetic factors (including metabolic genes) that modify the effectiveness of maternal tobacco cessation programs.

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Biostatistics & Research Epidemiology

Hensley Alford, S., K. Schwartz, A. Soliman, C. C. Johnson, S. B. Gruber and S. D. Merajver (2009). "Breast cancer characteristics at diagnosis and survival among Arab-American women compared to European- and African-American women." Breast Cancer Res Treat **114**(2): 339-46. **PDF Full-Text**

Henry Ford Hospital, Detroit, MI 48202, USA.

BACKGROUND: Data from Arab world studies suggest that Arab women may experience a more aggressive breast cancer phenotype. To investigate this finding, we focused on one of the largest settlements of Arabs and Iraqi Christians (Chaldeans) in the US, metropolitan Detroit- a SEER reporting site since 1973. MATERIALS AND METHODS: We identified a cohort of primary breast cancer cases diagnosed 1973-2003. Using a validated name algorithm, women were identified as being of Arab/Chaldean descent if they had an Arab last or maiden name. We compared characteristics at diagnosis (age, grade, histology, SEER stage, and marker status) and overall survival between Arab-, European-, and African-Americans. RESULTS: The cohort included 1,652 (2%) women of Arab descent, 13,855 (18%) African-American women, and 63,615 (80%) European-American women. There were statistically significant differences between the racial groups for all characteristics at diagnosis. Survival analyses overall and for each SEER stage showed that Arab-American women had the best survival, followed by European-American women. African-American women had the poorest overall survival and were 1.37 (95% confidence interval: 1.23-1.52) times more likely to be diagnosed with an aggressive tumor (adjusting for age, grade, marker status, and year of diagnosis). CONCLUSION: Overall, Arab-American women have a distribution of breast cancer histology similar to European-American women. In contrast, the stage, age, and hormone receptor status at diagnosis among Arab-Americans was more similar to African-American women. However, Arab-American women have a better overall survival than even European-American women.

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Cardiology

Alqaisi, F., F. Albadarin, Z. Jaffery, L. Tzogias, M. Dawod, G. Jacobsen and K. Ananthasubramaniam (2008). "Prognostic predictors and outcomes in patients with abnormal myocardial perfusion imaging and angiographically insignificant coronary artery disease." J Nucl Cardiol **15**(6): 754-61. **PDF Full-Text**

Heart and Vascular Institute, Henry Ford Hospital, Detroit, MI 48202, USA.

BACKGROUND: Abnormal stress myocardial perfusion imaging studies (SMPI) with angiographically insignificant coronary artery disease (ICAD) have often been labeled "false positive" scans. We evaluated the prognostic predictors and outcomes in an unselected patient population having abnormal SMPI and ICAD (study group) over a 24 month period of follow-up. METHODS: Retrospective study of consecutive patients who had SMPI and subsequent coronary angiography showing ICAD within 6 months of index scan with matched control group with normal scans. Major Adverse Cardiac Events (MACE) were defined as the first occurrence of death or myocardial infarction (MI). Patients were followed up to 24 months from the time of their SMPI to identify the development of MACE. RESULTS: One hundred and twenty five patients formed the study group and one hundred and thirty six patients formed the control group. Over a two-year follow up, approximately 13% of the study group had MACE as compared to 4.2% in the control group (P = .022).

Abnormal SMPI, EF < 40% and chronic kidney disease (GFR < 60 ml/min) were independent predictors of MACE in the study group. In multivariate analysis for MACE prediction, chronic kidney disease remained the sole independent predictor regardless of size or severity of perfusion abnormalities (P = <.001). CONCLUSION: Patients with abnormal SMPI and ICAD have a 13% event rate of MACE over a two-year follow up. CKD seems a very important marker of a higher risk subgroup amongst such patients.
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Cardiology
Clark, N. M., N. K. Janz, J. A. Dodge, X. H. Lin, B. L. Trabert, N. Kaciroti, L. Mosca, J. R. Wheeler and S. Keteyian (2009). "Heart Disease Management by Women: Does Intervention Format Matter?" Health Education & Behavior **36**(2): 394-409. **Article Request Form**

Univ Michigan, Ctr Managing Chron Dis, Ann Arbor, MI 48109 USA. Harvard Univ, Cambridge, MA 02138 USA. Univ Washington, Fred Hutchinson Canc Res Ctr, Seattle, WA 98195 USA. Columbia Univ, New York, NY USA. Henry Ford Hosp, Detroit, MI 48202 USA.

A randomized controlled trial of two formats of a program (Women Take PRIDE) to enhance management of heart disease by patients was conducted. Older women (N = 575) were randomly assigned to a group or self-directed format or to a control group. Data regarding symptoms, functional health status, and weight were collected at baseline and at 4, 12, and 18 months. The formats produced different outcomes. At 18 months, the self-directed format was better than the control in reducing the number (p <= .02), frequency (p <= .03), and bothersomeness (p <= .02) of cardiac symptoms. The self-directed format was also better than the group format in reducing symptom frequency of all types (p <= .04). The group format improved ambulation at 12 months (p <= .04) and weight loss at 18 months (p <= .03), and group participants were more likely to complete the program (p <= .05). The availability of different learning formats could enhance management of cardiovascular disease by patients.
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Cardiology
Flynn, K. E., I. L. Pina, D. J. Whellan, L. Lin, J. A. Blumenthal, S. J. Ellis, L. J. Fine, J. G. Howlett, S. J. Keteyian, D. W. Kitzman, W. E. Kraus, N. H. Miller, K. A. Schulman, J. A. Spertus, C. M. O'Connor and K. P. Weinfurt (2009). "Effects of Exercise Training on Health Status in Patients With Chronic Heart Failure HF-ACTION Randomized Controlled Trial." Jama-Journal of the American Medical Association **301**(14): 1451-1459. **PDF Full-Text**

Duke Univ, Sch Med, Duke Clin Res Inst, Ctr Clin & Genet Econ, Durham, NC 27715 USA. Duke Univ, Sch Med, Dept Psychiat & Behav Sci, Durham, NC 27715 USA. Duke Univ, Sch Med, Dept Med, Durham, NC 27715 USA. Case Western Reserve Univ, Sch Med, Dept Med, Cleveland, OH 44106 USA. Thomas Jefferson Univ, Jefferson Med Coll, Dept Med, Philadelphia, PA 19107 USA. NHLBI, Div Prevent & Populat Sci, Bethesda, MD 20892 USA. Stanford Univ, Dept Med, Stanford, CA 94305 USA. Dalhousie Univ, Queen Elizabeth Hlth Sci Ctr 2, Halifax, NS, Canada. Henry Ford Hosp, Div Cardiovasc Med, Detroit, MI 48202 USA. Wake Forest Univ, Sch Med, Dept Internal Med, Winston Salem, NC 27109 USA. St Lukes Hlth Syst, Mid Amer Heart Inst, Kansas City, MO USA. Univ Missouri Kansas City, Kansas City, MO USA.

Context Findings from previous studies of the effects of exercise training on patient-reported health status have been inconsistent. Objective To test the effects of exercise training on health status among patients with heart failure. Design, Setting, and Patients Multicenter, randomized controlled trial among 2331 medically stable outpatients with heart failure with left ventricular ejection fraction of 35% or less. Patients were randomized from April 2003 through February 2007. Interventions Usual care plus aerobic exercise training (n = 1172), consisting of 36 supervised sessions followed by home-based training, vs usual care alone (n = 1159). Randomization was stratified by heart failure etiology, which was a covariate in all models. Main Outcome Measures Kansas City Cardiomyopathy Questionnaire (KCCQ) overall summary scale and key

subscales at baseline, every 3 months for 12 months, and annually thereafter for up to 4 years. The KCCQ is scored from 0 to 100 with higher scores corresponding to better health status. Treatment group effects were estimated using linear mixed models according to the intention-to-treat principle. Results Median follow-up was 2.5 years. At 3 months, usual care plus exercise training led to greater improvement in the KCCQ overall summary score (mean, 5.21; 95% confidence interval, 4.42 to 6.00) compared with usual care alone (3.28; 95% confidence interval, 2.48 to 4.09). The additional 1.93-point increase (95% confidence interval, 0.84 to 3.01) in the exercise training group was statistically significant (P < .001). After 3 months, there were no further significant changes in KCCQ score for either group (P = .85 for the difference between slopes), resulting in a sustained, greater improvement overall for the exercise group (P < .001). Results were similar on the KCCQ subscales, and no subgroup interactions were detected. Conclusions Exercise training conferred modest but statistically significant improvements in self-reported health status compared with usual care without training. Improvements occurred early and persisted over time.

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Cardiology

Maltsev, V. A., J. W. Kyle and A. Undrovinas (2009). "Late Na(+) current produced by human cardiac Na(+) channel isoform Na (v)1.5 is modulated by its beta (1) subunit." J Physiol Sci **59**(3): 217-25. **Article Request Form**

Department of Internal Medicine, Cardiovascular Research, Henry Ford Hospital Detroit, Education and Research Bldg. Room 4015, 2799 West Grand Boulevard, Detroit, MI, 48202-2689, USA.

Experimental data accumulated over the past decade show the emerging importance of the late sodium current (I (NaL)) for the function of both normal and, especially, failing myocardium, in which I (NaL) is reportedly increased. While recent molecular studies identified the cardiac Na(+) channel (NaCh) alpha subunit isoform (Na(v)1.5) as a major contributor to I (NaL), the molecular mechanisms underlying alterations of I (NaL) in heart failure (HF) are still unknown. Here we tested the hypothesis that I (NaL) is modulated by the NaCh auxiliary beta subunits. tsA201 cells were transfected simultaneously with human Na(v)1.5 (former hH1a) and cardiac beta(1) or beta(2) subunits, and whole-cell patch-clamp experiments were performed. We found that I (NaL) decay kinetics were significantly slower in cells expressing alpha + beta(1) (time constant tau = 0.73 +/- 0.16 s, n = 14, mean +/- SEM, P < 0.05) but remained unchanged in cells expressing alpha + beta(2) (tau = 0.52 +/- 0.09 s, n = 5), compared with cells expressing Na(v)1.5 alone (tau = 0.54 +/- 0.09 s, n = 20). Also, beta(1), but not beta(2), dramatically increased I (NaL) relative to the maximum peak current, I (NaT) (2.3 +/- 0.48%, n = 14 vs. 0.48 +/- 0.07%, n = 6, P < 0.05, respectively) and produced a rightward shift of the steady-state availability curve. We conclude that the auxiliary beta(1) subunit modulates I (NaL), produced by the human cardiac Na(+) channel Na(v)1.5 by slowing its decay and increasing I (NaL) amplitude relative to I (NaT). Because expression of Na(v)1.5 reportedly decreases but beta(1) remains unchanged in chronic HF, the relatively higher expression of beta(1) may contribute to the known I (NaL) increase in HF via the modulation mechanism found in this study.

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Cardiology

O'Connor, C. M., D. J. Whellan, K. L. Lee, S. J. Keteyian, L. S. Cooper, S. J. Ellis, E. S. Leifer, W. E. Kraus, D. W. Kitzman, J. A. Blumenthal, D. S. Rendall, N. H. Miller, J. L. Fleg, K. A. Schulman, R. S. McKelvie, F. Zannad and I. L. Pina (2009). "Efficacy and Safety of Exercise Training in Patients With Chronic Heart Failure HF-ACTION Randomized Controlled Trial." Jama-Journal of the American Medical Association **301**(14): 1439-1450. **PDF Full-Text**

Duke Clin Res Inst, Durham, NC USA. Duke Univ, Sch Med, Dept Med, Durham, NC 27706 USA. Duke Univ, Sch Med, Dept Biostat & Bioinformat, Durham, NC 27706 USA. Duke Univ, Sch Med, Dept Psychiat & Behav Sci, Durham, NC 27706 USA. Thomas Jefferson Univ, Jefferson Med Coll, Dept Med, Philadelphia, PA 19107 USA. Henry Ford Hosp, Div Cardiovasc Med, Detroit, MI 48202 USA. NHLBI, Div Prevent & Populat Sci, Bethesda, MD 20892 USA. NHLBI, Div Cardiovasc Dis, Bethesda, MD 20892 USA. Wake Forest Univ, Sch Med, Dept Internal Med, Winston Salem, NC 27109 USA. Stanford Univ, Dept Med,

Stanford, CA 94305 USA. Hamilton Hlth Sci, Hamilton, ON, Canada. Univ Henri Poincare, Ctr Hosp Univ, INSERM, Ctr Invest Clin, Nancy, France. Case Western Reserve Univ, Sch Med, Dept Med, Cleveland, OH 44106 USA.

Context Guidelines recommend that exercise training be considered for medically stable outpatients with heart failure. Previous studies have not had adequate statistical power to measure the effects of exercise training on clinical outcomes. Objective To test the efficacy and safety of exercise training among patients with heart failure. Design, Setting, and Patients Multicenter, randomized controlled trial of 2331 medically stable outpatients with heart failure and reduced ejection fraction. Participants in Heart Failure: A Controlled Trial Investigating Outcomes of Exercise Training (HF-ACTION) were randomized from April 2003 through February 2007 at 82 centers within the United States, Canada, and France; median follow-up was 30 months. Interventions Usual care plus aerobic exercise training, consisting of 36 supervised sessions followed by home-based training, or usual care alone. Main Outcome Measures Composite primary end point of all-cause mortality or hospitalization and prespecified secondary end points of all-cause mortality, cardiovascular mortality or cardiovascular hospitalization, and cardiovascular mortality or heart failure hospitalization. Results The median age was 59 years, 28% were women, and 37% had New York Heart Association class III or IV symptoms. Heart failure etiology was ischemic in 51%, and median left ventricular ejection fraction was 25%. Exercise adherence decreased from a median of 95 minutes per week during months 4 through 6 of follow-up to 74 minutes per week during months 10 through 12. A total of 759 patients (65%) in the exercise training group died or were hospitalized compared with 796 patients (68%) in the usual care group (hazard ratio [HR], 0.93 [95% confidence interval {CI}, 0.84-1.02]; P=.13). There were nonsignificant reductions in the exercise training group for mortality (189 patients [16%] in the exercise training group vs 198 patients [17%] in the usual care group; HR, 0.96 [95% CI, 0.79-1.17]; P=.70), cardiovascular mortality or cardiovascular hospitalization (632 [55%] in the exercise training group vs 677 [58%] in the usual care group; HR, 0.92 [95% CI, 0.83-1.03]; P=.14), and cardiovascular mortality or heart failure hospitalization (344 [30%] in the exercise training group vs 393 [34%] in the usual care group; HR, 0.87 [95% CI, 0.75-1.00]; P=.06). In prespecified supplementary analyses adjusting for highly prognostic baseline characteristics, the HRs were 0.89 (95% CI, 0.81-0.99; P=.03) for all-cause mortality or hospitalization, 0.91 (95% CI, 0.82-1.01; P=.09) for cardiovascular mortality or cardiovascular hospitalization, and 0.85 (95% CI, 0.74-0.99; P=.03) for cardiovascular mortality or heart failure hospitalization. Other adverse events were similar between the groups. Conclusions In the protocol-specified primary analysis, exercise training resulted in nonsignificant reductions in the primary end point of all-cause mortality or hospitalization and in key secondary clinical end points. After adjustment for highly prognostic predictors of the primary end point, exercise training was associated with modest significant reductions for both all-cause mortality or hospitalization and cardiovascular mortality or heart failure hospitalization. …

Cardiology

Steinke, L., D. E. Lanfear, V. Dhanapal and J. S. Kalus (2009). "Effect of "Energy Drink" Consumption on Hemodynamic and Electrocardiographic Parameters in Healthy Young Adults." Annals of Pharmacotherapy **43**(4): 596-602. **PDF Full-Text**

Wayne State Univ, Detroit, MI USA. Henry Ford Hosp, Div Cardiol, Detroit, MI 48202 USA. Henry Ford Hosp, Dept Pharm Serv, Detroit, MI 48202 USA.

BACKGROUND: Energy drinks are frequently purported to improve cognitive function and concentration. However, the cardiovascular effects of these drinks have not been adequately studied. OBJECTIVE: component To determine the cardiac effects of a commercially available, multienergy drink in healthy volunteers. METHODS: Fifteen healthy adults were included in this prospective study. Individuals who had chronic medical conditions, were on chronic medication, or were pregnant or breast-feeding were excluded. Subjects abstained from caffeine for 48 hours prior to and during the study. In the morning on Day 1 of the study, while subjects were in a fasted state, baseline blood pressure (BP), heart rate (HR), and electrocardiographic (ECG) parameters were measured. Participants then consumed 500 mL (2 cans) of an energy drink and measurements were repeated 30 minutes, 1 hour, 2 hours, 3 hours, and 4 hours later. Participants then drank 500 mL of energy drink daily for the next 5 days. Day 1 protocol was repeated on Day 7. RESULTS: On Days 1 and 7, maximum mean systolic BP (SBP), HR, and QTc interval occurred at 4 hours. Maximum diastolic BP (DBP) occurred at 2 hours on Days 1 and 7. Within 4 hours of energy drink consumption, on Days 1 and 7, respectively, SBP increased by 7.9% ($p = 0.006$) and 9.6% ($p < 0.001$), HR increased by 7.8% ($p = 0.009$) and 11.0% ($p < 0.001$), and QTc interval increased by 2.4% ($p = 0.368$) and 5.0% ($p = 0.052$). DBP increased by 7.0% ($p = 0.046$) and 7.8% ($p = 0.063$) within 2 hours of energy drink

consumption on Days 1 and 7 respectively. CONCLUSIONS: Although no significant ECG changes were observed, HR increased 5-7 beats/min and SBP increased 10 mm Hg after energy drink consumption.
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Dermatology
Eide, M. J., R. Krajenta, D. Johnson, J. Long, G. Jacobsen and C. C. Johnson (2009). "Identification of patients with nonmelanoma skin cancer using HMO claims data." Journal of Investigative Dermatology **129**: 371. **PDF Meeting Abstract** (Scroll down to abstract #371)

Henry Ford Health System, Detroit, MI
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Dermatology
Germeroth, T. M., H. M. Gibson, A. J. Wilson, B. F. Chong and H. K. Wong (2009). "Loss of immune function genes and gain of non-lymphoid genes in Sezary Syndrome." Journal of Investigative Dermatology **129**: 197. **PDF Meeting Abstract** (Scroll down to abstract #197)

Henry Ford Health System, Detroit, MI.
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Dermatology
Gibson, H. M., T. M. Germeroth and H. K. Wong (2009). "Proteasome inhibitor differentially targets Rel-transcription factors to suppress type 1 genes and stimulate type 2 genes." Journal of Investigative Dermatology **129**: 531. **PDF Meeting Abstract** (Scroll down to abstract #531)

Henry Ford Hlth Syst, Detroit, MI USA. Wayne State Univ, Detroit, MI USA.
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Dermatology
Hexsel, C. L., M. J. Eide, C. C. Johnson, R. Krajenta, G. Jacobsen, I. Hamzavi and H. W. Lim (2009). "Incidence of nonmelanoma skin cancer in a cohort of patients with vitiligo." J Am Acad Dermatol **EPub Ahead of Print**. **PDF Full-Text**

Multicultural Dermatology Center, Department of Dermatology, Henry Ford Hospital, Detroit, Michigan.

BACKGROUND: Nonmelanoma skin cancer (NMSC) incidence in patients with vitiligo has not been studied. OBJECTIVE: We sought to quantify the incidence of NMSC in patients with vitiligo. METHODS: A cohort of 477 patients with vitiligo and no history of NMSC seen in an outpatient academic center between January 2001 and December 2006 was established. All charts for patients with vitiligo were reviewed for incident NMSC, and histopathology verified. Age-adjusted (2000 US Standard Million) incidence rates were calculated and compared to US rates. RESULTS: Six patients with NMSC were identified; all were Caucasian (>61 years). Age-adjusted incidence rates were: basal cell carcinoma, male 1382/100,000; basal cell carcinoma, female 0; squamous cell carcinoma, male 465/100,000; squamous cell carcinoma, female 156/100,000. Except for basal cell carcinoma in females, all rates were higher than US rates but not statistically significant. LIMITATIONS: Comparison incidence rates from the general patient population during the same time period were unavailable. CONCLUSION: Health care providers should be aware of the possible risk of NMSC in Caucasian patients with vitiligo.
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Dermatology

Hexsel, C. L., B. H. Mahmoud, D. Mitchell, J. Rivard, M. Owen, F. M. Strickland, H. W. Lim and I. Hamzavi (2009). "A clinical trial and molecular study of photoadaptation in vitiligo." Br J Dermatol **160**(3): 534-9. **PDF Full-Text**

Multicultural Dermatology Center, Department of Dermatology, Henry Ford Hospital, Detroit, MI 48202, USA.

BACKGROUND: Photoadaptation to ultraviolet (UV) B phototherapy is due to both pigmentary and nonpigmentary influences. OBJECTIVES: To measure photoadaptation in vitiliginous skin and to compare it with normal pigmented skin. METHODS: Seventeen patients with Fitzpatrick skin phototypes III-VI with vitiligo received six to nine UVB treatments, two to three times weekly. Minimal erythema dose (MED) testing was done at baseline and after all treatments; the percentage change in MED was analysed as a measure of photoadaptation. The percentage decrease in cyclobutane pyrimidine dimers (CPDs) over 24 h after a single exposure of 1 MED was analysed on vitiliginous and normal skin. RESULTS: The mean +/- SD percentage change in MED from before to after treatments was: treated vitiliginous skin 28.5 +/- 39.9% (P = 0.015), treated normal skin 35.9 +/- 49.9% (P = 0.015), untreated vitiliginous skin 11.9 +/- 22.6% (P =0.070), untreated normal skin 25.1 +/- 41.3% (P = 0.041). Of these patients, two-thirds had a positive percentage change in MED (photoadaptation). The mean amount of CPDs induced per megabase of DNA immediately after exposure was significantly higher in vitiliginous skin. The mean +/- SD percentage decrease in CPDs (rate of repair) in 24 h was 35.7 +/- 26.8% in vitiliginous skin (P = 0.027) and 46.2 +/- 19.5% in normally pigmented skin (P = 0.001); no difference was noted in the repair in vitiliginous skin compared with normal skin (P = 0.4). CONCLUSIONS: Photoadaptation in vitiliginous and normal skin was observed in two-thirds of patients. Vitiliginous skin had significantly more CPDs following UVB exposure; the rate of repair of UVB-induced DNA damage was equivalent to that in normal skin.

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Dermatology

Hexsel, D. M., T. Dal'Forno and C. L. Hexsel (2009). "A validated photonumeric cellulite severity scale." Journal of the European Academy of Dermatology and Venereology **23**(5): 523-528. **PDF Full-Text**

Univ Fed Rio Grande do Sul, Rio Grande Do Sul, Brazil. Univ Passo Fundo, Sch Med, Passo Fundo, Brazil. Henry Ford Hosp, Dept Dermatol, Detroit, MI 48202 USA.

With recent advances in the treatment of cellulite and localized fat, a comprehensive objective method of measuring cellulite can be potentially useful, especially since important morphological aspects of cellulite are not part of the current classification. To develop and to validate a new photonumeric cellulite severity. Based on standardized photographs of 55 patients with cellulite, five key morphological aspects of cellulite were identified. A new photonumeric severity scale was developed and validated. The five key morphological features of cellulite were identified and included the number of depressions, depth of depressions, clinical appearance of evident raised lesions, and presence of flaccidity and the grade of cellulite. Each item was graded from 0 to 3, allowing final classification of cellulite as mild, moderate, and severe. Results for validation of the scale are statistically significant (P < 0.05) and are as follows: intraclass correlation coefficient > 0.7; correlation item-total > 0.7, with the exception of the right buttock; intraclass correlation coefficients 0.881-0.922; Cronbach's alpha 0.851-0.989 and factor analysis 68-76%. The proposed photonumeric scale is a consistent, comprehensive, reliable, and reproducible tool for the standardized and objective assessment of the severity of cellulite. The authors hereby affirm that neither the manuscript nor any part of it has been published or is being considered for publication elsewhere.

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Dermatology

Huggins, R. H., L. A. Leithauser, M. J. Eide, C. L. Hexsel, G. Jacobsen and H. W. Lim (2009). "Assessment of quality of life of patient members of a web-based hydroa vacciniforme support group." Journal of Investigative Dermatology **129**: 370. **PDF Meeting Abstract** (Scroll down to abstract #370)

Henry Ford Hosp, Detroit, MI 48202 USA. Wayne State Univ, Sch Med, Detroit, MI USA.

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Dermatology
Kouba, D. J. (2008). Complications in Dermatologic Surgery. K. Nouri. Philadelphia, Mosby Yearbook Inc. WR 650 C7367 2008

Henry Ford Health System, Detroit, MI
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Dermatology
Lim, H. W. (2009). Clinical Guide to Sunscreens and Photoproection. New York, Informa Healthcare. QV 63 C641 2009
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Dermatology
Mahmoud, B. H., E. Ruvolo, C. Hexsel, Y. Liu, M. Owen, N. Kollias, H. W. Lim and I. H. Hamzavi (2009). "Photobiologic effects of long wavelength UVA and visible light on melanocompetent skin." Journal of Investigative Dermatology **129**: 750. **PDF Meeting Abstract**
(Scroll down to abstract #750)

Henry Ford Hosp, Detroit, MI 48202 USA. Johnson & Johnson, Consumer & Personal Prod Worldwide, Skillman, NJ USA.

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Dermatology
Mahmoud, B. H., A. Unnikrishnan, S. Siddiqui, D. J. Kouba, H. W. Lim, A. Heydari and I. H. Hamzavi (2009). "Controlled study on the relationship between vitamin D levels in tissue and blood in patients with non melanoma skin cancer." Journal of Investigative Dermatology **129**: 143. **PDF Meeting Abstract** (Scroll down to abstract #143)

Henry Ford Hosp, Detroit, MI 48202 USA. Wayne State Univ, Detroit, MI USA.
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Diagnostic Radiology
Akhondi-Asl, A. and H. Soltanian-Zadeh (2009). "Effect of Number of Coupled Structures on the Segmentation of Brain Structures." Journal of Signal Processing Systems for Signal Image and Video Technology **54**(1-3): 215-230. **Article Request Form**

Soltanian-Zadeh, H, Henry Ford Hosp, Radiol Image Anal Lab, 1 Ford Pl,2F, Detroit, MI 48202 USA. hamids@rad.hfh.edu

This paper reports the effect of the coupling information on the performance of model-based segmentation of the brain structures from magnetic resonance images (MRI). We have developed a three-dimensional, nonparametric, entropy-based, and multi-shape method that benefits from coupling of the shapes. The proposed method uses principal component analysis (PCA) to develop shape models that capture structural variability and integrates geometrical relationship among different structures into the algorithm by coupling them (limiting their independent deformations). At the same time, to allow variations of the coupled structures, it registers each structure individually when building the shape models. It defines an entropy-based energy function which is minimized using quasi-Newton algorithm. Probability density functions (pdf) are estimated iteratively using nonparametric Parzen window method. In the optimization algorithm, analytical derivatives are used for maximum speed and accuracy. Sample results are given for the segmentation of caudate, thalamus, putamen, pallidum, hippocampus, and amygdala illustrating superior performance of the proposed method

compared to the most similar method in the literature. The similarity of the results obtained by the proposed method with the expert segmentation is 4% to 12% higher than that of the most similar method. Experimental studies show that the proposed coupling method, which regulates shape variability during segmentation, improves accuracy of the results of the proposed method by 6% and those of the other method by 1%. In addition, the more the structures are used in the coupling process, the more accurate the results are obtained.
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Diagnostic Radiology
Flynn, M. (2008). Radiologic Science for Technologists. S. C. Bushong. St. Louis, MO, Mosby/Elsevier. WN 160 B979R 2008

Henry Ford Health System, Detroit, MI
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Diagnostic Radiology
Jain, R. and S. Patel (2008). Neuroscience in Medicine. P. M. Conn. Totawa, NJ, Humana Press. WL 102 N50594 2008

Henry Ford Health System, Detroit, MI
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Diagnostic Radiology
Kamer, A. P., J. G. Craig, M. T. van Holsbeeck and M. Abdulhak (2009). "An unusual presentation of a thoracic vertebral body fracture in a patient with diffuse idiopathic skeletal hyperostosis." J Trauma **66**(4): E57-60. **PDF Full-Text**

Henry Ford Hospital, Detroit, Michigan 48202, USA.
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Diagnostic Radiology
Liebeskind, D. S., S. R. Levine, H. J. Wang and S. C. Patel (2009). "Hyperdense Ischemic Infarcts in the NINDS rt-PA Trials Reflect Hyperglycemia, Not Hemorrhage." Stroke **40**(4): E117-E117. **Article Request Form** *Sladen Library has an electronic subscription, but the issue for this article was not available online at the time of this publication.*

Univ Calif Los Angeles, Los Angeles, CA USA. Mt Sinai Sch Med, New York, NY USA. Henry Ford Hlth Syst, Detroit, MI USA.
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Endocrinology & Metabolism
Akhter, N., B. Sinnott, K. Mahmood, S. Rao, S. Kukreja and E. Barengolts (2009). "Effects of vitamin D insufficiency on bone mineral density in African American men." Osteoporosis International **20**(5): 745-750. **PDF Full-Text**

Jesse Brown VA Med Ctr, Endocrinol Sect, Chicago, IL USA. Univ Illinois, Dept Med, Endocrinol Sect, Chicago, IL USA. Henry Ford Hosp, Detroit, MI 48202 USA. eibareng@uic.edu

In African American men serum, 25-hydroxyvitamin D (25-OHD) was below 30 ng/ml in 89% of subjects. In overall group, there was no correlation between 25-OHD and bone mineral density (BMD). A subgroup analysis of subjects with 25-OHD a parts per thousand currency sign15 ng/ml showed that serum 25-OHD was positively associated with BMD. This study examined the effects of low serum 25-hydroxyvitamin D (25-OHD) on bone mineral density (BMD) in African American (AA) men from the general medicine clinic at an inner city Veteran Administration medical center. The data for 112 AA males who had both 25-OHD levels and BMD of

spine and hip were extracted and analyzed using SAS software. AA men were aged 38 to 85 years, with mean age of 62 years. Levels of 25-OHD ranged from 4 to 45 ng/ml, with mean 17.5 ng/ml, 24% and 89% of the subjects had 25-OHD below 10 and 30 ng/ml, respectively. In the overall group, there was no correlation between 25-OHD and BMD at any site. In a subgroup analysis of subjects with 25-OHD a parts per thousand currency sign15 ng/ml, in multiple adjusted models, 25-OHD was positively associated with BMD of spine (r = 0.26, p = 0.05), total hip (r = 0.27, p < 0.05), ward's triangle (r = 0.25, p = 0.05), and trochanter (r = 0.30, p < 0.05). The negative effect of vitamin D insufficiency on bone was observed only at very low levels of 25-OHD, suggesting that AA male skeleton is relatively resistant to the effects of secondary hyperparathyroidism.
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Endocrinology & Metabolism

Cardenas, M. G., S. Kini and M. Wisgerhof (2009). "Two patients with highly aggressive macrofollicular variant of papillary thyroid carcinoma." Thyroid **19**(4): 413-6. **Article Request Form** *Sladen Library has an electronic subscription, but the issue for this article was not available online at the time of this publication.*

Division of Endocrinology, Diabetes and Bone and Mineral Disorders, Henry Ford Hospital, Detroit, Michigan 48202-3141, USA.

BACKGROUND: The macrofollicular variant of papillary thyroid carcinoma (MFV-PTC) is an unusual type of thyroid carcinoma with histological features that can be confused with nodular goiter or follicular adenoma. It generally has a good prognosis and low incidence of metastases. We report two patients with highly aggressive MFV-PTC including bone metastases, one of whom died of their disease. SUMMARY: The first patient was a 59-year-old woman with an occipital mass diagnosed histologically as papillary thyroid carcinoma (PTC), follicular variant. There were multiple bone lesions on computed tomography. Ten years earlier a biopsy of a thyroid nodule had been negative for malignant cells. Thyroidectomy showed a 3-cm nodule in the thyroid, diagnosed as MFV-PTC. Iodine 131 whole body scan showed uptake in the skull, ribs, thoracic and lumbar spine, and pelvic bones. The second patient was an 81-year-old man with a history of right thyroid nodule treated by total thyroidectomy with a postoperative diagnosis of adenomatous goiter. Three years later he developed a right shoulder mass, histologically diagnosed as follicular variant of PTC. The original thyroidectomy specimen was reviewed and reclassified as MFV-PTC. The patient developed new bone and lung metastases. Three treatments with (131)I were not effective. He died of metastatic thyroid cancer. CONCLUSIONS: To our knowledge these are the first cases of MFV-PTC reported with bone metastasis. Although MFV-PTC usually has a good prognosis these cases highlight the importance of careful histopathological examination for MFV-PTC in thyroidectomy specimens that may appear to be seemingly benign nodular thyroid disease.
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Endocrinology & Metabolism

Yu, Z. F., Z. A. Zhu, T. T. Tang, K. R. Dai and S. J. Qiu (2009). "Effect of body fat stores on total and regional bone mineral density in perimenopausal Chinese women." Journal of Bone and Mineral Metabolism **27**(3): 341-346. **PDF Full-Text**

Shanghai Jiao Tong Univ, Sch Med, Shanghai Peoples Hosp 9, Dept Orthopaed Surg, Shanghai 200011, Peoples R China. Henry Ford Hosp, Bone & Mineral Res Lab, Detroit, MI 48202 USA.

Accumulation of body fat is known to be beneficial to bone mass through increased body weight. However, not all the skeleton is loaded by body weight. Therefore, we assume that fat stores would exert different effects on bone mass at different skeletal sites. In this study, 84 perimenopausal Chinese women were recruited. Using dual-energy X-ray absorptiometry, total body fat mass (TBFM), total body lean mass (TBLM), percent body fat (PBF), and total body and regional bone mineral density (BMD) were measured. Correlation analysis indicated that PBF correlated negatively with BMD at ribs and both arms (all P < 0.05). After adjusting for TBLM, PBF had a significantly negative correlation with BMD at head, ribs, both arms, and whole body (all P < 0.05). With adjustment for body weight and height, a significantly negative correlation between PBF and BMD was present, not only at ribs and arms but also at legs and whole body (all P < 0.05, except right leg, at P = 0.094). There was a significantly positive correlation between body weight and leg BMD (all P < 0.001). Body weight was positively correlated with TBFM (r (2) = 0.783, P < 0.001) and TBLM (r (2) = 0.770, P < 0.001). Based on

the results, we conclude that increased body fat stores would exert a detrimental effect on BMD, but this effect is more prominent on non-weight-bearing bone. On weight-bearing bone, the detrimental effect of increased body fat could be offset or outweighed by the beneficial effect of increased body weight.

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Gastroenterology

Pisegna, J. R., R. G. Karlstadt, J. A. Norton, R. Fogel, D. S. Oh, G. J. Graepel and M. B. Dorr (2009). "Effect of Preoperative Intravenous Pantoprazole in Elective-Surgery Patients: A Pilot Study." Digestive Diseases and Sciences **54**(5): 1041-1049. **PDF Full-Text**

Univ Calif Los Angeles, CURE Digest Dis Res Ctr, Los Angeles, CA 90073 USA. VA Greater Los Angeles Healthcare Syst, Div Gastroenterol & Hepatol 691 111C, Los Angeles, CA 90073 USA. Univ Calif Los Angeles, Dept Med, Los Angeles, CA 90024 USA. Wyeth Pharmaceut, Global Med Affairs, Collegeville, PA USA. Stanford Univ, Dept Surg, Sch Med, San Francisco, CA USA. Henry Ford Hlth Syst, Div Gastroenterol, Detroit, MI USA.

Background This study evaluated the effects of intravenous pantoprazole on gastric volume and acid output in elective-surgical patients. Methods This is a multicenter, randomized, pilot study of adult patients receiving intravenous pantoprazole: 40 mg every 24 h, 40 mg every 12 h (q12h) or 80 mg q12h. The first dose was administered 1 h before general anesthesia for surgery. All gastric fluid was aspirated through a nasogastric tube 1 h before dosing and through the postoperative period. Aspirate volume was recorded; pH and H+ concentrations were measured. Result Twenty-six patients were enrolled and 21 were evaluable. Pantoprazole was well tolerated. All regimens decreased gastric acid output and volume, and increased pH within 1 h of dosing. Effects were sustained for up to 12 h following single-dose administration. Conclusions Intravenous pantoprazole administered prior to anesthesia induction may be efficacious for the reduction of gastric volume and acid output, and for pulmonary aspiration prophylaxis in surgical patients.

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Hypertension & Vascular Research

Li, X. C., Y. Shao and J. L. Zhuo (2009). "AT(1a) receptor knockout in mice impairs urine concentration by reducing basal vasopressin levels and its receptor signaling proteins in the inner medulla." Kidney Int **EPub Ahead of Print**. **Article Request Form**

Laboratory of Receptor and Signal Transduction, Division of Hypertension and Vascular Research, Department of Internal Medicine, Henry Ford Hospital, Detroit, Michigan, USA.

Angiotensin II plays an important role in the regulation of blood pressure, body salt and fluid balance, and urine concentration. Mice with deletion of the AT(1a) receptor develop polyuria and urine concentration defects. We studied the mechanisms of these urine concentration defects by treating wild-type and AT(1a)-knockout mice with arginine vasopressin (AVP) for 2 weeks, controlling their water intake, or giving them an osmotic diuretic (sucrose) in order to determine whether central or nephrogenic mechanisms were involved. Under basal conditions, AT(1a)-knockout mice were hypotensive, had lower plasma AVP, and excreted more urine with a markedly reduced osmolality compared with wild-type mice. However, basal glomerular filtration rates were similar in both strains of mice. We isolated total lysate and membrane proteins from the inner medulla of wild-type and mutant mouse kidneys, and found that the amounts of aquaporin 2 (AQP2), adenylyl cyclases III and V/VI, and phosphorylated MAP kinases ERK 1/2 proteins were all reduced in the inner medulla of the knockout mice. Infusion of AVP raised plasma levels and blood pressure proportionally in both strains, but polyuria persisted and urine osmolality remained significantly lower in the knockout mice. Although AVP increased urine osmolality slightly in water-deprived knockout mice, this was well below the basal osmolality of wild-type mice. The diuretic response to the hyperosmotic sucrose was also impaired in the knockout mice. Neither AVP nor water rationing restored the levels of the inner medullary signaling proteins and membrane AQP2 proteins in the knockout mice. We suggest that AT(1a) receptor deletion causes polyuria and urine concentration defects by decreasing basal AVP release and impairing AVP-induced receptor signaling in the inner medulla.

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Infectious Diseases

Johnson, L. E., K. Reyes and M. J. Zervos (2009). "Resources for infection prevention and control on the World Wide Web." Clin Infect Dis **48**(11): 1585-95. **PDF Full-Text**

Wayne State University School of Medicine, Division of Infectious Diseases, Henry Ford Hospital, Detroit, Michigan 48202, USA. ljohns14@hfhs.org

This review summarizes infection prevention resources on the Internet. Web sites are presented in 8 categories: guidelines, policies, and regulatory bodies; health care-associated infection and multidrug-resistant organisms; surveillance, reporting, and initiatives; antibiotic use; employee health; long-term care facilities; facility and environmental infection control; and professional societies, educational opportunities, and listserves. For example, links to the National Surgical Quality Improvement Program and National Healthcare Safety Network reports are provided among resources for infection surveillance, reporting, and initiatives. A link to guidelines for infection prevention in health care workers is listed with other information regarding employee health. The Web address for the Society for Healthcare Epidemiology of America guidelines for infection control in long-term care facilities is listed with resources for long-term care facilities. Guidelines for construction and environmental services are summarized with other information regarding facility and environmental infection control. This review summarizes the most useful and up-to-date infection prevention resources on the Internet and will simplify the search for pertinent information.

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Infectious Diseases

Zervos, M. (2008). "Treatment options for uncomplicated community-acquired skin and soft tissue infections caused by methicillin-resistant Staphylococcus aureus: oral antimicrobial agents." Surg Infect (Larchmt) **9 Suppl 1**: s29-34. **Article Request Form** *Sladen Library has an electronic subscription, but the issue for this article was not available online at the time of this publication.*

Division of Infectious Diseases, Department of Internal Medicine, Henry Ford Hospital, Detroit, Michigan 48202, USA. mzervos1@hfhs.org

BACKGROUND: In the United States, methicillin-resistant Staphylococcus aureus (MRSA) is a major cause of skin and soft tissue infections (SSTIs), and toxin-producing community-acquired MRSA (CA-MRSA) strains are becoming the leading cause of SSTIs presenting to emergency departments and outpatient settings. Many of these infections can be treated with oral antibiotics. This review is intended to delineate the types of SSTIs that require antibiotic treatment and to explain which CA-MRSA SSTIs can be treated with oral antibacterial agents. METHODS: Review of the literature related to the treatment of CA-MRSA SSTIs with oral antibacterial agents. RESULTS: Oral antimicrobial agents are available for the treatment of MRSA infection, and most SSTIs caused by CA-MRSA can be treated with these oral agents in an outpatient setting. Variable susceptibilities have been observed for CA-MRSA vs. hospital-acquired MRSA, pointing up the need for clinicians to be vigilant in determining susceptibility patterns. CONCLUSIONS: The growing prevalence of CA-MRSA in SSTIs and the increasing number of these infections observed in both the community and the hospital setting indicates that early, appropriate recognition and treatment are necessary. Many oral antimicrobial agents are available for the treatment of these infections.

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Internal Medicine

Massie, B. M., J. F. Collins, S. E. Ammon, P. W. Armstrong, J. G. F. Cleland, M. Ezekowitz, S. M. Jafri, W. F. Krol, C. M. O'Connor, K. A. Schulman, K. Teo and S. R. Warren (2009). "Randomized Trial of Warfarin, Aspirin, and Clopidogrel in Patients With Chronic Heart Failure The Warfarin and Antiplatelet Therapy in Chronic Heart Failure (WATCH) Trial." Circulation **119**(12): 1616-1624. **PDF Full-Text**

Dept Vet Affairs, San Francisco, CA USA. Vet Affairs Med Ctr, Cooperat Studies Program, Coordinating Ctr, Perry Point, MD USA. Univ Alberta, Edmonton, AB, Canada. Lankenau Inst Med Res, Wynnewood, PA USA. Henry Ford Hosp, Detroit, MI 48202 USA. Duke

Univ, Med Ctr, Durham, NC USA. McMaster Univ, Med Ctr, Hamilton, ON, Canada. Vet Affairs Med Ctr, Cooperat Studies Program Clin Res Pharm, Albuquerque, NM USA.

Background-Chronic heart failure remains a major cause of mortality and morbidity. The role of antithrombotic therapy in patients with chronic heart failure has long been debated. The objective of this study was to determine the optimal antithrombotic agent for heart failure patients with reduced ejection fractions who are in sinus rhythm. Methods and Results-This prospective, randomized clinical trial of open-label warfarin (target international normalized ratio of 2.5 to 3.0) and double-blind treatment with either aspirin (162 mg once daily) or clopidogrel (75 mg once daily) had a 30-month enrollment period and a minimum of 12 months of treatment. We enrolled 1587 men and women >= 18 years of age with symptomatic heart failure for at least 3 months who were in sinus rhythm and had left ventricular ejection fraction of <= 35%. The primary outcome was the time to first occurrence of death, nonfatal myocardial infarction, or nonfatal stroke. For the primary composite end point, the hazard ratios were as follows: for warfarin versus aspirin, 0.98 (95% CI, 0.86 to 1.12; P = 0.77); for clopidogrel versus aspirin, 1.08 (95% CI, 0.83 to 1.40; P=0.57); and for warfarin versus clopidogrel, 0.89 (95% CI, 0.68 to 1.16; P=0.39). Warfarin was associated with fewer nonfatal strokes than aspirin or clopidogrel. Hospitalization for worsening heart failure occurred in 116 (22.2%), 97 (18.5%), and 89 (16.5%) patients treated with aspirin, clopidogrel, and warfarin, respectively (P=0.02 for warfarin versus aspirin). Conclusion-The primary outcome measure and the mortality data do not support the primary hypotheses that warfarin is superior to aspirin and that clopidogrel is superior to aspirin.

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Internal Medicine

Tucciarone, M., P. A. Dileo, E. R. Castro and M. Guerrero (2009). "Myocardial Infarction Secondary to Carbon Monoxide Poisoning: An Uncommon Presentation of a Common Condition. Case Report and Review of the Literature." Am J Ther **EPub Ahead of Print**. **Article Request Form** *Sladen Library has an electronic subscription, but the issue for this article was not available online at the time of this publication.*

Department of Medicine, Henry Ford Hospital, Detroit, MI; Department of Medicine, Juan Maria de Salvatierra Hospital, La Paz, Baja California Sur, Mexico; and Division of Cardiology, Henry Ford Hospital, Detroit, MI.

Acute carbon monoxide poisoning is the most common cause of death from poisoning in the United States. It causes a spectrum of myocardial injury irrespective of carboxyhemoglobin levels and coronary anatomy. We present a 34-year-old woman with a non-ST-segment elevation myocardial infarction secondary to carbon monoxide poisoning who had normal coronary arteries by coronary angiography. A review of the literature is discussed.

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Neurology

Cui, X., M. Chopp, A. Zacharek, C. Roberts, Y. P. Yang and J. L. Chen (2009). "Critical Role of Endothelial Nitric Oxide Synthetase in Arteriogenesis after Stroke in Mice." Stroke **40**(4): E171-E171. **Article Request Form** *Sladen Library has an electronic subscription, but the issue for this article was not available online at the time of this publication.*

Henry Ford Hlth Syst, Detroit, MI USA.

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Neurology

Cui, Y. S., R. L. Zhang, L. Zhang, M. Lu, T. Schallert, M. Chopp and Z. G. Zhang (2009). "The Basket Test: Evaluating The Long Term Neurological Deficits After Focal Cerebral Ischemia In The Mouse." Stroke **40**(4): E168-E168. **Article Request Form** *Sladen Library has an electronic subscription, but the issue for this article was not available online at the time of this publication.*

Henry Ford Hosp, Detroit, MI 48202 USA. Univ Texas Austin, Austin, TX 78712 USA.
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Neurology
LeWitt, P. A. (2009). "MAO-B inhibitor know-how Back to the pharm." Neurology **72**(15): 1352-1357. **PDF Full-Text**

Henry Ford Hosp, Dept Neurol, Detroit, MI 48202 USA. Wayne State Univ, Sch Med, Dept Neurol, Detroit, MI 48201 USA.
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Neurology
LeWitt, P. A., W. G. Ondo, B. Van Lunen and P. B. Bottini (2009). "Open-Label Study Assessment of Safety and Adverse Effects of Subcutaneous Apomorphine Injections in Treating "Off" Episodes in Advanced Parkinson Disease." Clinical Neuropharmacology **32**(2): 89-93. **Article Request Form** *Sladen Library has an electronic subscription, but the issue for this article was not available online at the time of this publication.*

Wayne State Univ, Sch Med, Dept Neurol, Detroit, MI 48201 USA. Henry Ford Hosp, Detroit, MI 48202 USA. Baylor Coll Med, Dept Neurol, Houston, TX 77030 USA. Mylan Labs, Morgantown, WV USA.

Objective: To assess the safety and adverse effect profile of continued use of intermittent subcutaneous apomorphine to treat "off" episodes in subjects with advanced Parkinson disease. Methods: The study enrolled subjects with Hoehn and Yahr stage II-V Parkinson disease who were experiencing "off" events despite an optimized oral medication regimen. After baseline assessment and subcutaneous apomorphine dose titration (2-10mg/dose), subjects received >= 12 months of open-label treatment, as needed for "off" episodes. Results: Of the 546 Subjects in the study population, the majority used apomorphine on a daily basis; the average dose was 4.0 mg. A total of 187 subjects discontinued treatment because of adverse events (AEs). Most AEs were mild to moderate and expected with apomorphine. The AEs most commonly classified as definitely, probably, or possibly treatment related were nausea and vomiting, dyskinesia, dizziness, somnolence, hallucination, yawning, and injection site bruising. Serious AEs occurred in 199 subjects, but only 27 were considered to be probably or possibly treatment related. None of the 45 deaths recorded in the study were attributed to apomorphine. Conclusions: Long-term use of intermittent apomorphine dosing for treatment of "off" episodes was generally associated with mild-to-moderate AEs.
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Neurology
Liu, X. S., M. Chopp, X. G. Zhang, R. L. Zhang, B. Buller, A. Hozeska-Solgot, S. R. Gregg and Z. G. Zhang (2009). "Gene Profiles And Electrophysiology Of Doublecortin-expressing Cells In The Subventricular Zone After Ischemic Stroke." Stroke **40**(4): E139-E139. **Article Request Form** *Sladen Library has an electronic subscription, but the issue for this article was not available online at the time of this publication.*

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Neurology
Liu, Z. W., R. L. Zhang, Y. Li, Y. S. Cui and M. Chopp (2009). "Axonal Remodeling Of The Corticospinal Tract In The Denervated Side Of Spinal Cord Is Associated With Motor Recovery Following Ischemic Stroke In Adult Mice." Stroke **40**(4): E172-E172. **Article Request Form** *Sladen Library has an electronic subscription, but the issue for this article was not available online at the time of this publication.*

Henry Ford Hlth Syst, Detroit, MI USA.
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Neurology
Santra, M., S. Santra, C. Roberts, R. L. Zhang and M. Chopp (2009). "Doublecortin induces mitotic microtubule catastrophe and inhibits glioma cell invasion." J Neurochem **108**(1): 231-45. **PDF Full-Text**

Department of Neurology, Henry Ford Health System, Detroit, Michigan, USA.

Doublecortin (DCX) is a microtubule (MT) binding protein that induces growth arrest at the G2-M phase of cell cycle in glioma and suppresses tumor xenograft in immunocompromised hosts. DCX expression was found in neuronal cells, but lacking in glioma cells. We tested the hypothesis that DCX inhibits glioma U87 cell mitosis and invasion. Our data showed that DCX synthesizing U87 cells underwent mitotic MT spindle catastrophe in a neurabin II dependent pathway. Synthesis of both DCX and neurabin II were required to induce apoptosis in U87 and human embryonic kidney 293T cells. In DCX expressing U87 cells, association of phosphorylated DCX with protein phosphatase-1 (PP1) in the cytosol disrupted the interaction between kinesin-13 and PP1 in the nucleus and yielded spontaneously active kinesin-13. The activated kinesin-13 caused mitotic MT catastrophe in spindle checkpoint. Phosphorylated-DCX induced depolymerization of actin filaments in U87 cells, down-regulated matrix metalloproteinases-2 and -9, and inhibited glioma U87 cell invasion in a neurabin II dependent pathway. Thus, localization of the DCX-neurabin II-PP1 complex in the cytosol of U87 tumor cells inhibited PP1 phosphatase activities leading to anti-glioma effects via (1) mitotic MT spindle catastrophe that blocks mitosis and (2) depolymerization of actin that inhibits glioma cell invasion.
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Neurology
Shen, L. H., Y. Li and M. Chopp (2009). "Bone Marrow Stromal Cell Transplantation Enhances Glial Cell Derived Neurotrophic Factor Production, Facilitates Neuroblast Migration And Decreases Apoptosis In The Ischemic Boundary Zone After Stroke In Adult Rats." Stroke **40**(4): E216-E216. **Article Request Form** *Sladen Library has an electronic subscription, but the issue for this article was not available online at the time of this publication.*

Henry Ford Hosp, Detroit, MI 48202 USA.
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Neurology
Smith, B. (2008). Puzzling Cases of Epilepsy. D. Schmidt and S. C. Schachter. New York, Academic Press. WL 385 P99455 2008
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Neurology
Varelas, P. (2008). Acute Brain and Spinal Cord Injury. A. Bhardwaj, D. B. Ellegala and J. R. Kirsch. New York, Informa Healthcare. WL 354 A189 2008
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Neurology
Zacharek, A., X. Cui, M. Chopp and J. L. Chen (2009). "Effect of Stroke upon Endogenous Bone Marrow Stromal Cells." Stroke **40**(4): E210-E210. **Article Request Form** *Sladen Library has an electronic subscription, but the issue for this article was not available online at the time of this publication.*

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Neurology
Zhang, J., Y. Li, Z. G. Zhang, M. Lu, J. Borneman, B. Buller, S. Savant-Bhonsale, S. B. Elias and M. Chopp (2009). "Bone marrow stromal cells increase oligodendrogenesis after stroke." J Cereb Blood Flow Metab **EPub Ahead of Print**. **Article Request Form** *Sladen Library has an electronic subscription, but the issue for this article was not available online at the time of this publication.*

Department of Neurology, Henry Ford Health System, Detroit, Michigan, USA.

Oligodendrocytes are sensitive to ischemic damage. The Sonic hedgehog (Shh) pathway is critical in oligodendrogenesis; Gli1 is the principal effector of Shh signaling. We investigated oligodendrogenesis and Shh/Gli1 pathway activation after bone marrow stromal cell (BMSC) treatment of stroke in rats. Rats were subjected to the middle cerebral artery occlusion (MCAo). BMSCs have been shown to promote functional recovery post stroke. A therapeutic dose of BMSC (3 x 10(6) cells) treatment was initiated 1 day after MCAo. Immunohistochemistry was carried out to measure the oligodendrocyte progenitor cells, oligodendrocytes, myelin, and expressions of Shh and Gli1 at 14 days after MCAo. Gene expression of Shh and Gli1 was tested at 2 days after MCAo. An in vitro study was used to investigate the effects of BMSC on a premature oligodendrocyte cell line (N20.1 cells). BMSC treatment significantly increased O4(+) oligodendrocytes, MBP(+) area, and bromodeoxyuridine (BrdU)(+), NG2(+), BrdU(+)-NG2(+) cells, and mRNA and protein expressions of Shh and Gli1 in the ipsilateral brain of the MCAo rats than that in phosphate buffered saline (PBS)-treated rats. BMSCs promoted N20.1 cell proliferation and Gli1 mRNA expression, and these effects were abolished by the Shh pathway inhibitor cyclopamine. These data indicate that the BMSC treatment stimulates oligodendrogenesis by activation of the Shh/Gli1 pathway post stroke.
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Neurology
Zhang, L., Z. G. Zhang, Y. S. Cui, L. F. Jia and M. Chopp (2009). "Combination Of Atorvastatin And TPA Has A Neuroprotective Effect When Administered 6 h After Embolic Focal Ischemia In The Rat." Stroke **40**(4): E242-E242. **Article Request Form** *Sladen Library has an electronic subscription, but the issue for this article was not available online at the time of this publication.*

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Neurology
Zhang, R. L., Z. G. Zhang, S. R. Gregg, Y. Toh and M. Chopp (2009). "Neuroblasts In The Subventricular Zone Take Multiple Migratory Routes To Reach The Ischemic Striatum." Stroke **40**(4): E148-E148. **Article Request Form**

Henry Ford Health System, Detroit, MI
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Neurology
Zhang, Z. G. and M. Chopp (2009). "Neurorestorative therapies for stroke: underlying mechanisms and translation to the clinic." Lancet Neurol **8**(5): 491-500. **PDF Full-Text**

Department of Neurology, Henry Ford Hospital, Detroit, MI, USA.

Restorative cell-based and pharmacological therapies for experimental stroke substantially improve functional outcome. These therapies target several types of parenchymal cells (including neural stem cells, cerebral endothelial cells, astrocytes, oligodendrocytes, and neurons), leading to enhancement of endogenous neurogenesis, angiogenesis, axonal sprouting, and synaptogenesis in the ischaemic brain. Interaction between these restorative events probably underpins the improvement in functional outcome. This Review

provides examples of cell-based and pharmacological restorative treatments for stroke that stimulate brain plasticity and functional recovery. The molecular pathways activated by these therapies, which induce remodelling of the injured brain via angiogenesis, neurogenesis, and axonal and dendritic plasticity, are discussed. The ease of treating intact brain tissue to stimulate functional benefit in restorative therapy compared with treating injured brain tissue in neuroprotective therapy might more readily help with translation of restorative therapy from the laboratory to the clinic.

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Neurosurgery

Gusarova, G. A., L. A. Dada, A. M. Kelly, C. Brodie, L. A. Witters, N. S. Chandel and J. I. Sznajder (2009). "{alpha}1-AMP-activated protein kinase (AMPK) regulates hypoxia-induced Na,K-ATPase endocytosis via direct phosphorylation of PKC{zeta}." Mol Cell Biol **EPub Ahead of Print**. **Article Request Form**

Division of Pulmonary and Critical Care Medicine, Feinberg School of Medicine, Northwestern University, Chicago, IL, United States; Department of Neurosurgery and Hermelin Brain Tumor Center, Henry Ford Health System, Detroit, MI, USA; Departments of Medicine and Biochemistry, Dartmouth Medical School, and Department of Biological Sciences, Dartmouth College, Hanover, New Hampshire, USA.

Hypoxia promotes Na,K-ATPase endocytosis via PKCzeta-mediated phosphorylation of its alpha subunit. Here, we describe that hypoxia leads to phosphorylation of AMPK at Thr172 in rat alveolar epithelial cells. Over-expression of a dominant-negative AMPKalpha construct prevented the hypoxia-induced endocytosis of Na,K-ATPase. Overexpression of the reactive oxygen species (ROS) scavenger catalase prevented the hypoxia-induced AMPK activation. Moreover, hypoxia failed to activate AMPK in mitochondria-deficient A549-rho(0) cells, suggesting that mitochondrial ROS play an essential role in the hypoxia-induced AMPK activation. The hypoxia-induced PKCzeta translocation to the plasma membrane and phosphorylation at Thr410 was prevented by pharmacologically inhibiting AMPK or by over-expression of AMPK-DN construct. We found that AMPKalpha phosphorylates PKCzeta on residue Thr410 within the PKCzeta activation loop. Importantly, activation of AMPKalpha was necessary for hypoxia-induced AMPK-PKCzeta binding in alveolar epithelial cells. Overexpression of mutant PKCzeta-T410A prevented the hypoxia-induced Na,K-ATPase endocytosis, confirming that PKCzeta Thr410 phosphorylation is essential for this process. PKCzeta activation by AMPK is isoform specific as siRNA against the alpha1 but not the alpha2 catalytic subunit prevented PKCzeta activation. Accordingly, we provide first evidence that hypoxia-generated mitochondrial ROS lead to the activation of the AMPK alpha1 isoform, which binds and directly phosphorylates PKCzeta at Thr410, thereby promoting Na,K-ATPase endocytosis.

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Neurosurgery

Mikkelsen, T., C. Brodie, S. Finniss, M. E. Berens, J. L. Rennert, K. Nelson, N. Lemke, S. L. Brown, D. Hahn, B. Neuteboom and S. L. Goodman (2009). "Radiation sensitization of glioblastoma by cilengitide has unanticipated schedule-dependency." Int J Cancer **124**(11): 2719-27. **PDF Full-Text**

Department of Neurosurgery, Hermelin Brain Tumor Center, Henry Ford Hospital, Detroit, MI 48202, USA. nstom@neuro.hfh.edu

We investigated whether cilengitide could amplify the antitumor effects of radiotherapy in an orthotopic rat glioma xenograft model. Cilengitide is a specific inhibitor of alphav series integrins, and acts as an antiangiogenic. U251 human glioma cells express alphavbeta3 and alphavbeta5 integrins. We used in vitro assays of adhesion and growth of tumor and endothelial cells to evaluate cytotoxicity and the potential for cilengitide to enhance radiation toxicity. Treatment was then evaluated in an orthotopic model to evaluate synergy with therapeutic radiation in vivo. In vitro, cilengitide blocked cell adhesion, but did not influence the effects of radiation on U251 cells; cilengitide strongly amplified radiation effects on endothelial cell survival. In vivo, radiotherapy prolonged the survival of U251 tumor-bearing rats from 50 to over 110 days. Cotreatment with cilengitide and radiation dramatically amplified the effects of radiation, producing survival over 200 days and triggering an enhanced apoptotic response and suppression of tumor growth by histology at necropsy.

Signaling pathways activated in the tumor included NFkappab, a documented mediator of cellular response to radiation. Because cilengitide has a short plasma half-life (t((1/2)) approximately 20 min), antiangiogenic scheduling typically uses daily injections. We found that a single dose of cilengitide (4 mg/kg) given between 4 and 12 hr prior to radiation was sufficient to produce the same effect. Our results demonstrate that blockade of alphav integrins mediates an unanticipated rapid potentiation of radiation, and suggests possible clinical translation for glioma therapy.

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Neurosurgery

Nerenz, D. R. (2009). "Ethical issues in using data from quality management programs." Eur Spine J **EPub Ahead of Print**. **PDF Full-Text**

Department of Neurosurgery, Henry Ford Hospital, 2799 W. Grand Blvd. (K-11), Detroit, MI, 48202, USA, dnerenz1@hfhs.org.

Since the advent of formal, data-driven quality improvement programs in health care in the late 1980s and early 1990s, there are have been questions raised about requirements for ethical committee review of quality improvement activities. A form of consensus emerged through a series of articles published between 1996 and 2007, but there is still significant variation among ethics review committees and individual project leaders in applying broad policies on requirements for committee review and/or written informed consent by participants. Recent developments in quality management, particularly the creation and use of multi-site disease registries, have raised new questions about requirements for review and consent, since the activities often have simultaneous research and quality improvement goals. This article discusses ways in which policies designed for local quality improvement projects and data bases may be adapted to apply to multi-site registries and research projects related to them.

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Neurosurgery

Rosenblum, M. L., S. Kalkanis, W. Goldberg, J. Rock, T. Mikkelsen, S. Remer, S. Whitehouse and D. Nerenz (2009). "Odyssey of hope: a physician's guide to communicating with brain tumor patients across the continuum of care." J Neurooncol **92**(3): 241-51. **PDF Full-Text**

Department of Neurosurgery, Hermelin Brain Tumor Center, Henry Ford Hospital, 2799 West Grand Boulevard, Detroit, MI 48202, USA. mrosenb1@hfhs.org

The optimal treatment of a patient with a malignant brain tumor requires attention to the physical and emotional well-being of the affected individual and the family. We review the concept of hope as a critical support modality throughout the continuum of care for brain tumor patients and families. We offer suggestions based on our own observations over 17 years as well as the lessons taught to us by our patients and their families over that time and through a structured interview process.

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Neurosurgery

Xiong, Y., C. Qu, A. Mahmood, Z. Liu, R. Ning, Y. Li, D. L. Kaplan, T. Schallert and M. Chopp (2009). "Delayed transplantation of human marrow stromal cell-seeded scaffolds increases transcallosal neural fiber length, angiogenesis, and hippocampal neuronal survival and improves functional outcome after traumatic brain injury in rats." Brain Res **1263**: 183-91. **PDF Full-Text**

Department of Neurosurgery, Henry Ford Health System, Detroit, MI 48202, USA.

Traumatic brain injury (TBI) is a major cause of death and disability worldwide; however, no effective treatment has been clinically identified. Our recent studies show that the combination of collagen scaffolds with human bone morrow stromal cells (hMSCs) for treatment of TBI improves functional outcome and reduces the lesion volume when this combination was applied at day 4 after TBI in rats. The mechanisms underlying these

benefits remain unclear. Whether further delayed treatment with this combination will provide benefits has not been investigated. In the present study, we investigated whether the delayed (7 days post injury) transplantation would have beneficial effects on functional and histological outcome and sought to elucidate underlying mechanisms of therapeutic action. Collagen scaffolds seeded with 3 x 10(6) hMSCs, scaffolds alone, 3 x 10(6) hMSCs alone, or saline were transplanted into the lesion cavity of the injured cortex 7 days after TBI. Sensorimotor function and spatial learning were measured. Corticocortical labeling with 1, 1''-dioleyl-3, 3, 3'', 3''-tetramethylindocarbocyanine methanesulfonate (DiI) was performed at day 36 after TBI. The rats were sacrificed 43 days after TBI, and the brain tissue was processed for DiI-labeling fiber and immunohistochemical analyses. The present data show that delayed transplantation of hMSCs or scaffolds seeded with hMSCs improved spatial learning and sensorimotor function, enhanced angiogenesis in the injured cortex and the ipsilateral hippocampus and increased DiI-labeled neural fiber length in the injured cortex. hMSC-seeded scaffolds may be a new and effective way to improve neurological function after TBI.
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Otolaryngology
Stach, B. (2008). Pediatric Audiology: Diagnosis, Technology, and Management. J. R. Madell and C. Flexer. New York, Thieme. WV 271 P3715 2008
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Pathology
Pan, S., R. Chen, B. A. Reimel, D. A. Crispin, H. Mirzaei, K. Cooke, J. F. Coleman, Z. Lane, M. P. Bronner, D. R. Goodlett, M. W. McIntosh, W. Traverso, R. Aebersold and T. A. Brentnall (2009). "Quantitative proteomics investigation of pancreatic intraepithelial neoplasia." Electrophoresis **30**(7): 1132-1144. **PDF Full-Text**

Univ Washington, Dept Med, Seattle, WA 98195 USA. Univ Washington, Dept Pathol, Seattle, WA 98195 USA. Inst Syst Biol, Seattle, WA USA. Cleveland Clin Fdn, Dept Anat Pathol, Cleveland, OH 44195 USA. Henry Ford Hosp, Dept Anat Pathol, Detroit, MI 48202 USA. Univ Washington, Dept Med Chem, Seattle, WA 98195 USA. Fred Hutchinson Canc Res Ctr, Mol Diagnost Program, Seattle, WA 98104 USA. Virginia Mason Med Ctr, Seattle, WA 98101 USA. Univ Zurich, Fac Sci, CH-8006 Zurich, Switzerland. ETH, Inst Mol Syst Biol, Zurich, Switzerland.

Patients with pancreatic cancer are usually diagnosed at late stages, when the disease is incurable. Pancreatic intraepithelial neoplasia (PanIN) 3 is believed to be the immediate precursor lesion of pancreatic adenocarcinoma, and would be an ideal stage to diagnose patients, when intervention and cure are possible and patients are curable. In this study, we used quantitative proteomics to identify dysregulated proteins in PanIN 3 lesions. Altogether, over 200 dysregulated proteins were identified in the PanIN 3 tissues, with a minimum of a 1.75-fold change compared with the proteins in normal pancreas. These dysregulated PanIN 3 proteins play roles in cell motility, the inflammatory response, the blood clotting cascade, the cell cycle and its regulation, and protein degradation. Further network analysis of the proteins identified c-MYC as an important regulatory protein in PanIN 3 lesions. Finally, three of the overexpressed proteins, laminin beta-1, galectin-1, and actinin-4 were validated by immunohistochemistry analysis. All three of these proteins were overexpressed in the stroma or ductal epithelial cells of advanced PanIN lesions as well as in pancreatic cancer tissue. Our findings suggest that these three proteins may be useful as biomarkers for advanced PanIN and pancreatic cancer if further validated. The dysregulated proteins identified in this study may assist in the selection of candidates for future development of biomarkers for detecting early and curable pancreatic neoplasia.
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Pathology
Zarbo, R. (2007). Oral Pathology. J. A. Regezi, J. J. Sciubba and R. C. K. Jordan. St. Louis, MO, Saunders/Elsevier. WU 140 R333 2007
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Pulmonary

Burke, R. R., C. H. Stone, S. Havstad and B. A. Rybicki (2009). "Racial differences in sarcoidosis granuloma density." Lung **187**(1): 1-7. **PDF Full-Text**

Division of Pulmonary, Critical Care and Sleep Medicine, Henry Ford Hospital, Detroit, MI 48202, USA. rburke1@hfhs.org

STUDY OBJECTIVES: While sarcoidosis generally inflicts a greater morbidity on African-American compared with Caucasian patients, no studies have examined whether racial differences exist in the intensity of the histologic hallmark of sarcoidosis, noncaseating granulomas. DESIGN AND SETTING: The study was conducted as a retrospective case series in a tertiary referral center. PATIENTS: The study included 187 patients with histopathologic confirmation of sarcoidosis by trans- and/or endobronchial biopsy between July 1991 and December 2001. MEASUREMENTS AND RESULTS: Granuloma density was the average number of granulomas per biopsy piece on the slide with the most intense granulomatous inflammation at fourfold magnification. Overall, African-American patients had a twofold greater median granuloma density than Caucasians (p = 0.005). In a negative binomial multivariate model, radiographic pattern had the strongest association with granuloma density, with Scadding stage II and III patients having adjusted granuloma densities of 60% (p = 0.005) and 105% (p = 0.0001) higher than stage I patients. In the specific-tissue types, radiographic stage-adjusted granuloma densities in African-American patients were 49% greater in bronchial tissue (p = 0.03), but only a 27% greater in alveolar tissue (p = 0.51). CONCLUSIONS: A greater granuloma density in bronchiolar lung tissue of African-American sarcoidosis patients may explain racial differences in diagnostic yield by lung biopsy and disease severity at diagnosis. This association persists even after controlling for Scadding radiographic stage, a measure of disease severity strongly associated with granuloma density.

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Pulmonary

Khalid, I., I. Obeid, B. DiGiovine, U. Khalid and Z. Q. Morris (2009). "Predictive value of sGaw, FEF(25-75), and FEV1 for development of asthma after a negative methacholine challenge test." J Asthma **46**(3): 284-90. **Article Request Form**

Division of Pulmonary and Critical Care Medicine, Henry Ford Hospital, Detroit, Michigan, USA. dr.imrankhalid@yahoo.com

BACKGROUND: A 20% change in forced expiratory volume in 1 second (FEV(1)) during methacholine challenge testing (MCT) is a reliable marker of asthma. When the FEV(1) decrease is < 20%, there is controversy whether other changes in flows and conductance may be useful. We conducted this study to determine whether changes in sGaw, FEF(25 - 75), and FEV(1) in a negative MCT could predict future occurrence of asthma over a 3-year period. METHODS: A total of 100 consecutive patients with clinical suspicion of asthma but who had a negative MCT per ATS FEV(1) criteria (< 20% FEV(1) decline at 16 mg/mL of methacholine) performed by the 5-breath dosimeter method were analyzed. Two pulmonary fellows, blinded to MCT results, reviewed the patients' medical records. Patients were classified into one of three categories: asthmatic, unclear, and not asthmatic. Decreases in sGaw, FEF(25 - 75), and FEV(1) in the five groups were then retrieved. Analysis of variance (ANOVA) was used for data analysis. RESULTS: Of 100 patients, 23 were excluded owing to lack of a 3-year follow-up. After complete data review, the number of patients (n) in each group was as follows: asthmatic (n = 15), unclear (n = 7), and not asthmatic (n = 55). sGaw and FEF(25 - 75) decreases from the negative MCT could not predict asthma; however, decreases in FEV(1) were associated with future asthma occurrence (sGaw p = 0.21, FEF25-75 p = 0.07, FEV(1) p = 0.0009). Forty-three percent of the patients who had a 10% to 20% decline in FEV(1) eventually developed asthma. CONCLUSION: Up to 20% of patients who have symptoms suggestive of asthma but a negative MCT can still develop asthma. Declines in sGaw and FEF(25 - 75) in a negative MCT appear to have no clinical significance. A decrease in FEV(1), especially 10% to 20%, is associated with the diagnosis of future asthma.

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Pulmonary

Truesdell, S. (2008). Respiratory Nursing: A Core Curriculum. M. Geiger-Bronsky and D. Wilson. New York, Springer Pub. Co. WY 163 R4344 2008

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Radiation Oncology

Siddiqui, F., M. Patel, M. Khan, S. McLean, J. Dragovic, J. Y. Jin, B. Movsas and S. Ryu (2009). "Stereotactic Body Radiation Therapy for Primary, Recurrent, and Metastatic Tumors in the Head-and-Neck Region." Int J Radiat Oncol Biol Phys **EPub Ahead of Print**. **PDF Full-Text**

Department of Radiation Oncology, Head and Neck Surgery, Henry Ford Health System, Detroit, MI.

PURPOSE: To determine the feasibility, safety, and efficacy of stereotactic body radiation therapy (SBRT), also known as radiosurgery, in patients with head-and-neck cancers. METHODS AND MATERIALS: Patients with pathologically proven malignant lesions in the head-and-neck region were treated using single-dose SBRT (S-SBRT) or fractionated SBRT (F-SBRT). Radiation doses were either single-fraction 13-18 Gy for S-SBRT or 36-48 Gy in five to eight fractions for F-SBRT. Response evaluation was based on clinical examinations and computed tomography/magnetic resonance imaging scans. Pre- and post-SBRT tumor dimensions were measured in three axes, and tumor volumes were calculated. Response evaluation also was performed using World Health Organization criteria. RESULTS: Fifty-five lesions were treated in 44 patients (25 men, 19 women). There were three groups of patients: those with primary (n = 10), recurrent (n = 21), and metastatic tumors (n = 13). The predominant histologic type was squamous cell carcinoma (n = 33). The majority of lesions were treated using F-SBRT (n = 37). Based on radiographic and clinical assessment, a 77% (complete + partial response) response rate was noted. Percentage of reduction in tumor volume was 52% +/- 38% based on follow-up scans in 24 patients. Tumor control rates at 1 year were 83.3% and 60.6% in the primary and recurrent groups, respectively. Median overall survival was 28.7, 6.7, and 5.6 months for the primary, recurrent, and metastatic groups, respectively. Radiation Therapy Oncology Group Grade 1-2 mucositis was noted in all patients treated for oropharyngeal or laryngeal lesions. CONCLUSIONS: The SBRT in single or fractionated doses offers a viable treatment option for selected patients with primary, recurrent, and metastatic head-and-neck cancers with functional preservation.

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Rheumatology

Cheng, X., D. G. Haggins, R. H. York, Y. N. Yeni and O. Akkus (2009). "Analysis of Crystals Leading to Joint Arthropathies by Raman Spectroscopy: Comparison with Compensated Polarized Imaging." Applied Spectroscopy **63**(4): 381-386. **Article Request Form**

Purdue Univ, Weldon Sch Biomed Engn, W Lafayette, IN 47907 USA. Henry Ford Hosp, Dept Rheumatol, Taylor, MI 48180 USA. Beale Inst, Lansing, MI 48917 USA. Henry Ford Hosp, Dept Orthopaed & Rehabil, Ctr Bone & Joint, Detroit, MI 48202 USA.

The current study, assessed the feasibility of the application of Raman spectroscopy toward the diagnosis of gout and pseudogout. First, the lowest concentrations of monosodium urate monohydrate (MSUM) and calcium pyrophosphate dihydrate (CPPD) crystals detectable by Raman spectroscopy were investigated by Mixing known amounts of synthetic crystals with synovial fluid in the concentration range of 1 to 100 mu g/mL. Second. a digestion protocol was developed for clinical samples to improve crystal extraction. The ensuing centrifugation of the digest congregated crystals at a well-defined point and allowed for point-and-shoot Raman analysis without having to conduct an extensive search for individual crystals. Finally. synovial fluid samples obtained from patients (n = 35) were cross-analyzed by polarized light microscopy (PLM) and the Raman method to compare and contrast the diagnoses of the two methods. It was found that Raman spectroscopy call detect MSUM and CPPD crystals with good sensitivity and specificity at concentrations as low as 5 mu g/mL, and 2.5 mu g/mL, respectively using the current method. This detection limit of Raman analysis is lower than that reported for PLM. Raman and PLM diagnoses of clinical samples agreed in 32 out of 35 samples in the entire sample pool. However, the rate of disagreement between PLM-based and Raman-based diagnoses was noteworthy within the subset of diseased samples (3 out of 10). indicating that PLM has limitations and that the confirmation by a secondary method is essential for a reliable outcome. The proposed protocol of sample preparation in[] Raman analysis ascribes baseline feasibility to the diagnosis of gout and pseudogout by Raman spectroscopy, thus justifying further studies using a larger clinical sample set for obtaining sensitivity and specificity.

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Sleep Medicine
Richardson, G. and S. Wang-Weigand (2009). "Effects of long-term exposure to ramelteon, a melatonin receptor agonist, on endocrine function in adults with chronic insomnia." Hum Psychopharmacol **24**(2): 103-11. **PDF Full-Text**

Henry Ford Hospital, Sleep Disorders and Research Center, Detroit, MI 48202, USA. grichar1@hfhs.org

OBJECTIVE: To evaluate the effects of ramelteon, an MT(1)/MT(2) melatonin receptor agonist used to treat insomnia, on endocrine function in adults with chronic insomnia. METHODS: This was a double-blind, placebo-controlled, trial of adults (18-45 years) with chronic insomnia. Subjects received either ramelteon 16 mg or placebo nightly for 6 months. Hormonal measures of the thyroid, reproductive, and adrenal axes were analyzed monthly and compared with baseline and placebo values. RESULTS: While isolated changes were detected at some time points, there were no consistent statistically significant differences between treatments on measures of thyroid function (total T4, free T4, TSH, and total T3), adrenal function (AM cortisol, and ACTH), or on most reproductive endocrine measures [LH, FSH, estradiol (women), total, and free testosterone (men)]. Prolactin concentrations were increased overall in women in the ramelteon group compared with placebo (p = 0.003). No clinical effects of elevated prolactin were reported; average menstrual cycle length, duration of menses, and ovulation probability did not differ between groups. CONCLUSIONS: Long-term exposure to ramelteon 16 mg, a potent melatonin receptor agonist, resulted in mild, transient increase in prolactin, in women only, that were not associated with measurable reproductive effects. There were no consistent changes in other endocrine measures.
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Sleep Medicine
Roehrs, T. and T. Roth (2008). Sleep Disorders: Diagnosis and Therapeutics. S. R. Pandi-Perumal, J. C. Verster and J. M. Monti. London, Informa Healthcare. WM 188 S6322 2008
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Surgery
Brandt, M. M., I. Rubinfeld, J. Jordan, D. Trivedi and H. M. Horst (2009). "Transfusion insurgency: practice change through education and evidence-based recommendations." Am J Surg **197**(3): 279-83. **PDF Full-Text**

Department of Surgery, Henry Ford Hospital, Detroit, MI, USA. mbrandt1@hfhs.org

BACKGROUND: In 2000, we implemented an evidence-based guideline in the surgical intensive care unit (SICU) using a transfusion threshold of hemoglobin <8 g/dL. We hypothesized that continual education on the transfusion protocol would decrease transfusions. METHODS: We analyzed 2-month samples of admissions in even-numbered years from 1998 to 2006. Any infusion of packed red blood cells (PRBCs) was included. RESULTS: We analyzed data from 2,138 patients resulting in 5,130 transfusions. Thirty-six patients received >20 U of blood. The only difference between groups occurred in 2006 when renal failure increased. Transfusions decreased from 3.2 +/- 0.34 (SE) to 1.7 +/- 0.2. The number of patients who received blood also decreased. Mortality and length of stay (LOS) were not different among the groups. Every unit of blood transfused increased the mortality risk by 14%. CONCLUSIONS: Implementation of an evidence-based transfusion guideline reduced the number of infused units and patients transfused without an increase in mortality.
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Surgery
Harrington, C. B., A. Siddiqui and M. Feuerstein (2009). "Workstyle As a Predictor of Pain and Restricted Work Associated With Upper Extremity Disorders: A Prospective Study." Journal of Hand Surgery-American Volume **34A**(4): 724-731. **PDF Full-Text**

Uniformed Serv Univ Hlth Sci, Dept Med & Clin Psychol, Bethesda, MD 20814 USA. Henry Ford Hosp, Div Plast Surg, Detroit, MI 48202 USA.

Purpose: A patient's reaction to a perceived increase in work demand may be related to his or her upper limb symptoms. The purpose of this study was to determine whether a brief measure of a patient's perception of how they respond to perceived increases in demands at work predicts pain levels and work status 6 months after an initial consultation with a hand surgeon. Methods Working patients with diverse upper extremity diagnoses completed a measure of response to job stress at their first clinic visit and were followed for 6 months during their prescribed treatment course. Controlling for age, gender, job type, diagnosis, patient perceptions of work-relatedness, baseline pain, grip strength, and treatment (surgery vs no surgery) analyses were conducted to determine whether self-reported response to perceived job stress was associated with pain and work status 6 months after the initial consultation. Results Higher scores on the patient-reported job stress measure predicted higher levels of pain at 6 months. The measure was also a modest but significant predictor of work status at 6 months. Conclusions Evaluation of a working patient's self-reported cognitive and behavioral response to perceived increases in work demands, or what has been referred to as workstyle, predicts subsequent levels of upper extremity pain and work status. Generalization to other practice settings requires further study. This measure provides a brief evaluation of reaction to job stress that can be an important factor in certain patients with upper extremity symptoms. Future controlled studies addressing this aspect of the clinical picture are indicated.

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Surgery

Oliveira, C., J. Senz, P. Kaurah, H. Pinheiro, R. Sanges, A. Haegert, G. Corso, J. Schouten, R. Fitzgerald, H. Vogelsang, G. Keller, S. Dwerryhouse, D. Grimmer, S. F. Chin, H. K. Yang, C. E. Jackson, R. Seruca, F. Roviello, E. Stupka, C. Caldas and D. Huntsman (2009). "Germline CDH1 deletions in hereditary diffuse gastric cancer families." Human Molecular Genetics **18**(9): 1545-1555. **PDF Full-Text**

British Columbia Canc Agcy, Hereditary Canc Program, Vancouver, BC V5Z 4E6, Canada. British Columbia Canc Agcy, Ctr Translat & Appl Genom, Vancouver, BC V5Z 4E6, Canada. Univ Porto IPATIMUP, Inst Mol Pathol & Immunol, P-4200465 Oporto, Portugal. Univ Porto, Fac Med, P-4200319 Oporto, Portugal. CBM Scrl, I-34012 Trieste, Italy. Prostate Ctr Microarray Facil, Vancouver, BC V6H 3Z6, Canada. Univ Siena, ITT, Translat Res Lab, Dept Human Pathol & Oncol,Sect Surg Oncol, I-53100 Siena, Italy. Univ Siena, Div Surg Oncol, I-53100 Siena, Italy. MRC Holland, NL-1057 DN Amsterdam, Netherlands. Hutchinson MRC Res Ctr, MRC Canc Cell Unit, Cambridge CB2 0XZ, England. Tech Univ Munich, Dept Surg, D-81675 Munich, Germany. Tech Univ Munich, Inst Pathol, D-81675 Munich, Germany. Univ Cambridge, Dept Oncol, Cambridge CB2 0QQ, England. Li Ka Shing Ctr, Canc Res UK Cambridge Res Inst, Cambridge CB2 0RE, England. [Yang, Han-Kwang] Seoul Natl Univ, Coll Med, Dept Surg, Seoul 151742, South Korea. Seoul Natl Univ, Coll Med, Canc Res Inst, Seoul 151742, South Korea. Henry Ford Hosp, Dept Surg, Detroit, MI 48202 USA. Henry Ford Hosp, Dept Med Genet, Detroit, MI 48202 USA.

Germline CDH1 point or small frameshift mutations can be identified in 30-50% of hereditary diffuse gastric cancer (HDGC) families. We hypothesized that CDH1 genomic rearrangements would be found in HDGC and identified 160 families with either two gastric cancers in first-degree relatives and with at least one diffuse gastric cancer (DGC) diagnosed before age 50, or three or more DGC in close relatives diagnosed at any age. Sixty-seven carried germline CDH1 point or small frameshift mutations. We screened germline DNA from the 93 mutation negative probands for large genomic rearrangements by Multiplex Ligation-Dependent Probe Amplification. Potential deletions were validated by RT-PCR and breakpoints cloned using a combination of oligo-CGH-arrays and long-range-PCR. In-silico analysis of the CDH1 locus was used to determine a potential mechanism for these rearrangements. Six of 93 (6.5%) previously described mutation negative HDGC probands, from low GC incidence populations (UK and North America), carried genomic deletions (UK and North America). Two families carried an identical deletion spanning 193 593 bp, encompassing the full CDH3 sequence and CDH1 exons 1 and 2. Other deletions affecting exons 1, 2, 15 and/or 16 were identified. The statistically significant over-representation of Alus around breakpoints indicates it as a likely mechanism for these deletions. When all mutations and deletions are considered, the overall frequency of CDH1 alterations in HDGC is similar to 46% (73/160). CDH1 large deletions occur in 4% of HDGC families by mechanisms involving mainly non-allelic homologous recombination in Alu repeat sequences. As the finding of pathogenic

CDH1 mutations is useful for management of HDGC families, screening for deletions should be offered to at-risk families.

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Urology

Boris, R. S., A. Bhandari, L. S. Krane, D. Eun, S. Kaul and J. O. Peabody (2009). "Salvage robotic-assisted radical prostatectomy: initial results and early report of outcomes." BJU Int **103**(7): 952-6. **PDF Full-Text**

Vattikuti Urology Institute, Henry Ford Health System, Detroit, MI 48202, USA.

OBJECTIVE: To evaluate the initial results of salvage robotic-assisted radical prostatectomy (SRARP) after recurrence following primary radiotherapy (RT) for localized prostate cancer. PATIENTS AND METHODS: Between December 2002 and January 2008, 11 patients had SRARP with pelvic lymph node dissection by one surgeon from one institution. Six patients had brachytherapy, three had external beam RT (EBRT), one intensity-modulated RT, and one received brachytherapy with an EBRT boost. All patients had prostate cancer on biopsy after RT, with negative computed tomography and bone scan. The mean (range) follow-up was 20.5 (1-77) months. RESULTS: The mean interval from RT to SRARP was 53.2 months; the mean preoperative prostate-specific antigen (PSA) level was 5.2 ng/mL, the operative duration 183 min and the estimated blood loss 113 mL. One patient had prolonged lymphatic drainage, one had an anastomotic leak, and one had an anastomotic stricture requiring direct vision internal urethrotomy at 3 months. The mean duration of catheterization was 10.4 days and the hospital stay 1.4 days. Three patients had a biochemical recurrence, at 1, 2 and 43 months. In one of two patients with node-positive carcinoma of the prostate the PSA level failed to reach a nadir of zero after surgery. In patients with a minimum follow-up of 2 months, eight of 10 are continent (defined as zero to one pad per day) and two have erections adequate for intercourse with the use of phosphodiesterase-5 inhibitors. CONCLUSION: SRARP after RT-resistant disease recurrence is feasible with minimal perioperative morbidity. Early functional outcomes appear to be at least equivalent with historical salvage RP series. Robotic extended pelvic lymph node dissection is safe and can improve the accuracy of surgical staging. A longer follow-up is necessary to better assess the functional and oncological outcomes.

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Urology

Laungani, R. G., N. Seleno and A. M. Carlin (2008). "Effect of laparoscopic gastric bypass surgery on urinary incontinence in morbidly obese women." Surg Obes Relat Dis **EPub Ahead of Print**. **Article Request Form**

Vattikuti Urology Institute, Henry Ford Health System, Detroit, MI.

BACKGROUND: Morbid obesity is an independent risk factor for urinary incontinence (UI) that tends to be underreported. A validated, reliable, self-administered, easy-to-use questionnaire was used to determine the effect of laparoscopic gastric bypass (LGB) surgery on UI in morbidly obese women. METHODS: We prospectively evaluated 470 morbidly obese women seeking bariatric surgery with the International Consultation on Incontinence Questionnaire Short Form. The International Consultation on Incontinence Questionnaire Short Form was given to female patients at their initial consultation and at 3 and 12 months after LGB to assess both UI symptoms and quality of life. Data are expressed as the mean +/- standard deviation. RESULTS: The preoperative prevalence of UI was 66% (n = 309) and included 21% urge, 33% stress, and 46% mixed UI. For the 58 patients with UI who underwent LGB and completed a follow-up International Consultation on Incontinence Questionnaire Short Form, a reduction occurred in the total symptom score from 7.6 +/- 4 preoperatively to 3.0 +/- 4 and 1.8 +/- 4 ($P < .001$) at 3 and 12 months after LGB, respectively. The corresponding quality-of-life scores improved from 3.2 +/- 3 to 1.0 +/- 2 and 0.4 +/- 2 ($P < .001$). The UI had resolved in 64% and improved overall in 92% of patients at 1 year after LGB. An improvement in UI was found within 3 months after LGB with as little as 30 lb of weight loss. CONCLUSION: UI is a common co-morbidity in the morbidly obese and was prevalent in two thirds of female patients presenting for bariatric surgery evaluation. LGB with resultant weight loss significantly improved the UI symptoms and quality of life.

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Urology

Menon, M. and J. Brown (2008). Treatment Methods for Early and Advanced Prostate Cancer. R. S. Kirby, A. W. Partin and J. K. Parsons. London, Informa Healthcare. WJ 762 T784 2008

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Urology

Patil, N., L. Krane, K. Javed, T. Williams, M. Bhandari and M. Menon (2009). "Evaluating and grading cystographic leakage: correlation with clinical outcomes in patients undergoing robotic prostatectomy." BJU Int **103**(8): 1108-10. **PDF Full-Text**

Vattikuti Urology Institute, Henry Ford Hospital, Detroit, MI 48202, USA. npatil1@hfhs.org

OBJECTIVE: To classify cystographically detected urinary leaks in patients undergoing computer-assisted (robotic) radical prostatectomy (RP) and to evaluate its effect on postoperative outcomes. PATIENTS AND METHODS: Between October 2001 and October 2007, 3327 patients had a RP using a technique described previously. The data were entered prospectively into an approved database. Before catheter removal, all patients had a gravity cystogram taken 7 days after RP. All patients who had a detectable urinary leak on cystography were stratified into three groups by two independent radiologists using a previously described grading system. Patients were evaluated with a validated International Prostate Symptom Score at 3-, 6-, 9- and 12-month intervals after RP. The continence status was determined based on a patient-reported questionnaire. Medical records in these patients were reviewed for the presence of complications requiring secondary interventions. RESULTS: In all, 287 patients (8.6%) had a detectable leak on cystography, of which 179 (62.4%), 84 (29.3%) and 24 (8.4%) were grades I, II and III, respectively. Of the patients with a detectable leak 70% were continent within 3 months and 94% had no involuntary urinary leakage at 1 year. Eight of 287 (2.8%) patients required a secondary intervention to correct bladder neck contracture. All eight of these patients had a grade II or III leak on cystography. CONCLUSION: The presence of a urinary leak might delay the time to continence, but has no adverse effect on long-term urinary control. Quantifying the gradation of leakage according to the described classification might provide the clinician with prognostic information about patients at risk for future interventions.

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