

Henry Ford Health System Publication List October 2009

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

Biostatistics & Research Epidemiology

Alford, S. M. H., R. E. Lappin, L. Peterson and C. C. Johnson (2009). "Pregnancy Associated Smoking Behavior and Six Year Postpartum Recall." Maternal and Child Health Journal **13**(6): 865-872. [PDF Full-Text](#)

[Alford, Sharon M. Hensley; Lappin, Rachel E.; Peterson, L.; Johnson, Christine C.] Henry Ford Hlth Syst, Dept Biostat & Res Epidemiol, Detroit, MI 48202 USA. Alford, SMH, Henry Ford Hlth Syst, Dept Biostat & Res Epidemiol, 1 Ford Pl, Suite 5C-BRE, Detroit, MI 48202 USA. salford1@hfhs.org

Background This study examined predictors and behaviors of pregnancy-related smoking among women who belonged to a private health maintenance organization and the recall accuracy of pregnancy-related smoking behaviors after 6-years. **Methods** A cohort of 725 pregnant women was followed for six years. Major predictors for smoking behavior before, during, and one-year following pregnancy were determined. In addition, accuracy of recall six years postpartum of smoking behavior at the time of pregnancy and one-year postpartum was tested. **Results** Mother's education, asthma status, amount of pre-pregnancy smoking, gravidity, and father's smoking status were important in the prediction of pregnancy associated smoking. Agreement for recall of smoking behavior during pregnancy (6 year recall) and one-year postpartum (5 year recall) were 90% and 91%, respectively. **Conclusions** Despite potentially adverse outcomes, a proportion of women continue to smoke throughout pregnancy. A number of variables proved to be important predictors of pregnancy associated smoking behavior. These factors should be considered by smoking cessation programs targeting women of reproductive age. Additionally, there was substantial agreement for maternal recall at six years postpartum of smoking behavior at the time of pregnancy and one-year postpartum. This should be considered in retrospective study designs that are primarily based on maternal recall of smoking behaviors before, during, and following pregnancy.

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Biostatistics & Research Epidemiology

Cassidy-Bushrow, A. E., L. F. Bielak, A. D. Rule, P. F. Sheedy, S. T. Turner, V. D. Garovic and P. A. Peyser (2009). "Hypertension during pregnancy is associated with coronary artery calcium independent of renal function." J Womens Health (Larchmt) **18**(10): 1709-16. [Article Request Form](#)

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BACKGROUND: Hypertension during pregnancy (HDP) increases the risk of future coronary heart disease (CHD), but it is unknown whether this association is mediated by renal injury. Reduced renal function is both a complication of HDP and a risk factor for CHD. **METHODS:** Logistic regression models were fit to examine the association between a history of HDP and the presence and extent of coronary artery calcification (CAC), a measure of subclinical coronary artery atherosclerosis, in 498 women from the Epidemiology of Coronary Artery Calcification Study (mean age 63.3 +/- 9.3 years). **RESULTS:** Fifty-two (10.4%) women reported a history of HDP. After adjusting for age at time of study participation, HDP was associated with increased serum creatinine later in life ($p = 0.014$). HDP was positively associated with the presence of CAC after adjusting for age at time of study participation ($OR = 2.7$, 95% CI 1.4-5.4). This association was slightly attenuated with adjustment for body size and blood pressure ($OR = 2.4$, 95% CI 1.2-4.9) but was not further attenuated with adjustment for serum creatinine and urinary albumin/creatinine ratio ($OR = 2.6$, 95% CI 1.3-5.3). Results were similar for CAC extent. **CONCLUSIONS:** HDP may increase a woman's risk of future CHD beyond traditional risk factors and renal function. Women with a history of HDP should be monitored for potential increased risk of CHD as they age.

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Bone & Joint Center

Guzman-Morales, J., H. El-Gabalawy, M. H. Pham, N. Tran-Khanh, M. D. McKee, W. Wu, M. Centola and C. D. Hoemann (2009). "Effect of chitosan particles and dexamethasone on human bone marrow stromal cell osteogenesis and angiogenic factor secretion." *Bone* **45**(4): 617-626. [PDF Full-Text](#)

[Guzman-Morales, Jessica; Pham, Minh H.; Tran-Khanh, Nicolas; Hoemann, Caroline D.] Ecole Polytech, Dept Chem Engrn, Montreal, PQ H3C 3A7, Canada. [El-Gabalawy, Hani] Univ Manitoba, Rheumat Dis Res Lab, Winnipeg, MB, Canada. [McKee, Marc D.] McGill Univ, Fac Dent, Montreal, PQ, Canada. [McKee, Marc D.] McGill Univ, Dept Anat & Cell Biol, Montreal, PQ, Canada. [Wu, William] Henry Ford Hosp, Ctr Bone & Joint, Detroit, MI 48202 USA. [Centola, Michael] Univ Oklahoma, Hlth Sci Ctr, Dept Microbiol & Immunol, Oklahoma City, OK 73190 USA. [Hoemann, Caroline D.] Ecole Polytech, Inst Biomed Engrn, Montreal, PQ H3C 3A7, Canada.

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Chitosan is a polysaccharide scaffold used to enhance cartilage repair during treatments involving bone marrow stimulation, and it is reported to increase angiogenesis and osteogenesis in vivo. Here, we tested the hypotheses that addition of chitosan particles to the media of human bone marrow stromal cell (BMSC) cultures stimulates osteogenesis by promoting osteoblastic differentiation and by favoring the release of angiogenic factors in vitro. Confluent BMSCs were cultured for 3 weeks with 16% fetal bovine serum, ascorbate-2-phosphate and disodium beta-glycerol phosphate, in the absence or presence of dexamethasone, an anti-inflammatory glucocorticoid commonly used as an inducer of BMSC osteoblast differentiation in vitro. As expected, dexamethasone slowed cell division, Stimulated alkaline phosphatase activity and enhanced matrix mineralization. Added chitosan particles accumulated intra- and extracellularly and, while not affecting most osteogenic features, they inhibited osteocalcin release to the media at day 14 and interfered with mineralized matrix deposition. Interestingly, dexamethasone promoted cell attachment and suppressed the release and activation of matrix metalloproteinase-2 (MMP-2). While chitosan particles had no effect on the release of angiogenic factors, dexamethasone significantly inhibited ($p < 0.05$ to $p < 0.0001$) the release of vascular endothelial growth factor (VEGF), granulocyte-macrophage colony stimulating factor (GM-CSF), tumor necrosis factor-alpha (TNF-alpha), interleukins 1 beta, 4, 6, and 10 (IL-beta, IL-4, IL-6, IL-10), and a host of other inflammatory factors that were constitutively secreted by BMSCs. These results demonstrate that chitosan particles alone are not sufficient to promote osteoblast differentiation of BMSCs in vitro, and suggest that chitosan promotes osteogenesis in vivo through indirect mechanisms. Our data further show that continuous addition of dexamethasone promotes osteoblastic differentiation in vitro partly by inhibiting gelatinase activity and by suppressing inflammatory cytokines which result in increased cell attachment and cell cycle exit. (c) 2009 Elsevier Inc. All rights reserved.

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Bone & Joint Center

Ninh, C. C., A. Sethi, M. Hatahet, C. Les, M. Morandi and R. Vaidya (2009). "Hip dislocation after modular unipolar hemiarthroplasty." *J Arthroplasty* **24**(5): 768-74. [PDF Full-Text](#)

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An institutional review board-approved retrospective review of hip fractures in elderly patients treated with a modular unipolar implant was carried out to identify factors predisposing to dislocation of a hemiarthroplasty. The main outcome measure evaluated was dislocation vs nondislocation. Two hundred seventeen patients underwent the surgery, and 174 were available for review at 6 weeks and 144 at 1 year. The incidence of dislocation was 6%. The average time of dislocation after surgery was 19.3 days. Clinical factors significant for dislocation were male sex and mental disease. Radiographic factors in dislocated hips included a smaller femoral neck and contralateral femoral neck offset. The center edge angle was also smaller in the dislocated patients. These patients had a higher mortality rate.

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Cardiology

Atchley, A. E., D. W. Kitzman, D. J. Whellan, A. E. Iskandrian, S. J. Ellis, R. A. Pagnanelli, A. Kao, K. Abdul-Nour, C. M. O'Connor, G. Ewald, W. E. Kraus and S. Borges-Neto (2009). "Myocardial perfusion, function, and dyssynchrony in patients with heart failure: Baseline results from the single-photon emission computed tomography imaging ancillary study of the Heart Failure and A Controlled Trial Investigating Outcomes of Exercise TraiNing (HF-ACTION) Trial." *American Heart Journal* **158**(4): S53-S63. [PDF Full-Text](#)

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Background There are currently limited data on the relationships between resting perfusion abnormalities, left ventricular ejection fraction (LVEF), New York Heart Association (NYHA) functional class, and exercise capacity as defined by peak VO₂ and 6-minute walk test in patients with heart failure (HF) and reduced LVEF. Furthermore, the association between resting perfusion abnormalities and left ventricular dyssynchrony is currently unknown. This article addresses the Heart Failure and A Controlled Trial Investigating Outcomes of Exercise TraiNing (HF-ACTION) gated SPECT imaging (gSPECT) substudy baseline results. **Methods** HF-ACTION was a multicenter, randomized controlled trial of aerobic exercise training versus usual care in 2,331 stable patients with LVEF of ≤ 35% and NYHA class II to IV HF symptoms treated with optimal medical therapy. Subjects enrolled in the HF-ACTION substudy underwent resting Tc-99m tetrofosmin gSPECT at baseline (n = 240). Images were evaluated for extent and severity of perfusion abnormalities using a 17-segment and a 5-degree gradation severity score (summed rest score [SRS]). Left ventricular function and dyssynchrony were assessed using validated available commercial software. **Results** The average age of patients enrolled was 59, 69% were male, 63% were white, and 33% were African American. Of the 240 participants, 129 (54%) were ischemic and 111 (46%) were nonischemic in etiology. The median LVEF by gSPECT for the entire cohort was 26%. Among the nuclear variables, there was a modest correlation between LVEF and SRS (r=-0.31, P<.0001) and there were stronger correlations between phase SD and SRS (r=0.66, P<.0001) as well as phase SD and LVEF (r=-0.50, P<.0001). Patients with NYHA class III symptoms had more severe and significant degrees of dyssynchrony (median phase SD 54 degrees) than those with NYHA class II symptoms (median phase SD 39 degrees, P=.001). Patients with an ischemic etiology had a higher SRS (P<.0001) and significantly more dyssynchrony (P<.0001) than those who were nonischemic. However, there was no difference in LVEF or objective measures of exercise capacity between these groups. With respect to peak VO₂, there was a weak correlation with LVEF (r=0.18, P=.006) and no correlation with SRS (r=-0.04, P=0.59) or with dyssynchrony (r=-0.13, P=.09). A weak but statistically significant correlation between SRS and 6-minute walk was observed (r=-0.15, P=.047). **Conclusions** Gated SPECT imaging can provide important information in patients with HIF due to severe LV dysfunction including quantitative measures of global systolic function, perfusion, and dyssynchrony. These measurements are modestly but significantly related to symptom severity and objective measures of exercise capacity. (Am Heart J 2009; 158:S53-S63.)

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Cardiology

Bronas, U. G., A. T. Hirsch, T. Murphy, D. Badenhop, T. C. Collins, J. K. Ehrman, A. G. Ershow, B. Lewis, D. J. Treat-Jacobson, M. E. Walsh, N. Oldenburg and J. G. Regensteiner (2009). "Design of the multicenter standardized supervised exercise training intervention for

the 'CLAudication: Exercise Vs Endoluminal Revascularization (CLEVER) study'." [Vascular Medicine](#) **14**(4): 313-321. [Article Request Form](#)

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The CLAudication: Exercise Vs Endoluminal Revascularization (CLEVER) study is the first randomized, controlled, clinical, multicenter trial that is evaluating a supervised exercise program compared with revascularization procedures to treat claudication. In this report, the methods and dissemination techniques of the supervised exercise training intervention are described. A total of 217 participants are being recruited and randomized to one of three arms: (1) optimal medical care; (2) aortoiliac revascularization with stent; or (3) supervised exercise training. Of the enrolled patients, 84 will receive supervised exercise therapy. Supervised exercise will be administered according to a protocol designed by a central CLEVER exercise training committee based on validated methods previously used in single center randomized control trials. The protocol will be implemented at each site by an exercise committee member using training methods developed and standardized by the exercise training committee. The exercise training committee reviews progress and compliance with the protocol of each participant weekly. In conclusion, a multicenter approach to disseminate the supervised exercise training technique and to evaluate its efficacy, safety and cost-effectiveness for patients with claudication due to peripheral arterial disease (PAD) is being evaluated for the first time in CLEVER. The CLEVER study will further establish the role of supervised exercise training in the treatment of claudication resulting from PAD and provide standardized methods for use of supervised exercise training in future PAD clinical trials as well as in clinical practice.

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Cardiology

Gupta, R. C. and H. N. Sabbah (2009). "Expression of H11 Kinase Is Increased in Left Ventricular Myocardium of Explanted Failed Human Hearts and in Hearts of Dogs with Experimentally Induced Heart Failure." [Circulation Research](#) **105**(7): P40. [Article Request Form](#)

[Gupta, Ramesh C.; Sabbah, Hani N.] Henry Ford Hosp, Detroit, MI 48202 USA.

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Cardiology

Keteyian, S. J., D. Isaac, U. Thadani, B. A. Roy, D. R. Bensimhon, R. McKelvie, S. D. Russell, A. S. Hellkamp and W. E. Kraus (2009). "Safety of symptom-limited cardiopulmonary exercise testing in patients with chronic heart failure due to severe left ventricular systolic dysfunction." [American Heart Journal](#) **158**(4): S72-S77. [PDF Full-Text](#)

[Keteyian, Steven J.] Henry Ford Hosp, Div Cardiovasc Med, Detroit, MI 48202 USA. [Isaac, Debra] Foothills Prov Gen Hosp, Calgary, AB T2N 2T9, Canada. [Thadani, Udho] Univ Oklahoma, Hlth Sci Ctr, Vet Adm Med Ctr, Oklahoma City, OK USA. [Roy, Brad A.] Summit Med Fitness Ctr, Kalispell Reg Med Ctr, Kalispell, MT USA. [Bensimhon, Daniel R.] LeBauer Cardiovasc Res Fdn, Durham, NC USA. [McKelvie, Robert] Hamilton Hlth Sci, Hamilton, ON, Canada. [Russell, Stuart D.] Johns Hopkins Univ, Div Cardiol, Baltimore, MD USA. [Hellkamp, Anne S.; Kraus, William E.] Duke Univ, Med Ctr, Durham, NC USA. [Hellkamp, Anne S.; Kraus, William E.] Duke Clin Res Inst, Durham, NC USA.

Background To assess the safety of symptom-limited exercise testing inpatients with New York Heart Association class II-IV heart failure symptoms due to left ventricular systolic dysfunction, we investigated the frequency of all-cause fatal and nonfatal major cardiovascular (CV) events among subjects enrolled in a prospective clinical trial (HF-ACTION). We hypothesized that exercise testing would be safe, as defined by a rate for all-cause death of <0.1 per 1 000 tests and a rate of nonfatal CV events <1.0 per 1,000 tests. **Methods** Before enrollment and at 3, 12, and 24 months after randomization, subjects were scheduled to complete a symptom-limited graded exercise test with open-circuit spirometry for analysis of expired gases. To ensure the accurate reporting of exercise test-related events, we report deaths and nonfatal major CV events per 1 000 tests at months 3, 12, or 24 after randomization. **Results** A total of 2,331 subjects were randomized into HF-ACTION. After randomization, 2,037 subjects completed 4,411 exercise tests. There were no test-related deaths, exacerbation of heart failure or angina requiring hospitalization, myocardial infarctions, strokes, or transient ischemic attacks. There was one episode each of ventricular fibrillation and sustained ventricular tachycardia. There were no exercise test-related implantable cardioverter defibrillator discharges requiring hospitalization. These findings correspond to zero deaths per 1,000 exercise tests and 0.45 nonfatal major CV events per 1,000 exercise tests (95% CI 0.11-1.81). **Conclusions** In New York Heart Association class II-IV patients with severe left ventricular systolic dysfunction, we observed that symptom-limited exercise testing is safe based on no deaths and a rate of nonfatal major CV events that is <0.5 per 1,000 tests. (Am Heart J 2009; 158:572-S77.)

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Cardiology

Pahle, A. S., D. Sorli, T. Omland, C. W. Knudsen, A. Westheim, A. H. B. Wu, P. G. Steg, J. McCord, R. M. Nowak, J. E. Hollander, A. B. Storrow, W. T. Abraham, P. A. McCullough and A. Maisel (2009). "Impact of Systemic Hypertension on the Diagnostic Performance of B-Type Natriuretic Peptide in Patients With Acute Dyspnea." *American Journal of Cardiology* **104**(7): 966-971. [PDF Full-Text](#)

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Hypertension may affect the diagnostic performance of B-type natriuretic peptide (BNP). The objective of the present study was to assess the impact of a history of hypertension or blood pressure elevation on admission on the diagnostic performance of BNP in the diagnosis of heart failure (HF) in patients with acute dyspnea. BNP levels were measured using a rapid point-of-care device in 1,586 patients with acute dyspnea. In patients with HF, BNP levels did not differ between those with and without histories of hypertension. Conversely, in patients without HF, a history of hypertension was associated with higher median BNP levels (38 pg/ml [interquartile range 13 to 1191 vs 21 pg/ml [interquartile range 7 to 64], $p < 0.001$). The areas under the receiver-operating characteristic curves were 0.88 and 0.93 for those with and without histories of hypertension, respectively ($p < 0.001$). Blood pressure elevation on admission did not affect the diagnostic accuracy of BNP (areas under the curve 0.90 in the 2 groups). In conclusion, although a history of hypertension is associated with higher BNP levels in patients with acute dyspnea without HF, the impact on the overall diagnostic performance of BNP is modest. Accordingly, BNP performs well as an indicator of HF in patients presenting in emergency departments regardless of a history of hypertension or elevated blood pressure on admission. (C) 2009 Elsevier Inc. All rights reserved. (Am J Cardiol 2009;104:966-971)

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Cardiology

Palevo, G., S. J. Keteyian, M. Kang and J. L. Caputo (2009). "Resistance Exercise Training Improves Heart Function and Physical Fitness in Stable Patients With Heart Failure." Journal of Cardiopulmonary Rehabilitation and Prevention **29**(5): 294-298. [PDF Full-Text](#)

[Palevo, Gregory] RehabCare Grp, St Louis, MO 63105 USA. [Palevo, Gregory] St Thomas Hosp, Dept Cardiac Hlth & Rehabil, Nashville, TN USA. [Keteyian, Steven J.] Henry Ford Hosp, Div Cardiovasc Med, Detroit, MI 48202 USA. [Kang, Minsoo; Caputo, Jennifer L.] Middle Tennessee State Univ, Dept Hlth & Human Performance, Murfreesboro, TN 37130 USA.

Palevo, G, RehabCare Grp, 7733 Forsyth Blvd, Ste 2300, St Louis, MO 63105 USA.

PURPOSE: This study determined the effect of a structured isotonic strength training (ST) program on left ventricular (LV) function (ejection fraction, stroke volume, and end-diastolic and end-systolic volumes) and physical fitness (6-minute walk test, upper body strength, lower body strength, and body composition) in patients with New York Heart Association class II and III heart failure. **METHODS:** Sixteen patients were randomized into 2 groups., ST and Usual care The ST group) 0 0 patients) performed 24 ST exercise sessions (3 per week, 8 weeks), while the usual care (6 patients) group followed routine medical care The structure isotonic ST program involved 12 different exercise.,; on circuit Weight machines LV function OD echocardiography) and physical fitness were assessed at baseline and 8 weeks **RESULTS:** Modest improvements ($P < .05$) in resting ejection fraction (0.32-0.37) and stroke volume (46 to 53 mL/beat), as well as in muscular strength and 6-minute walk distance, were found after training **CONCLUSIONS:** A short-term structured isotonic ST program appears to improve selected measures of resting I-V function and fitness in patients with mild congestive heart failure Additional studies utilizing larger numbers of subjects, including women, are needed

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Cardiology

Pina, I. L., P. Kokkinos, A. Kao, V. Bittner, M. Saval, B. Clare, L. Goldberg, M. Johnson, A. Swank, H. Ventura, G. Moe, M. Fitz-Gerald, S. J. Ellis, M. Vest, L. Cooper and D. Whellan (2009). "Baseline differences in the HF-ACTION trial by sex." American Heart Journal **158**(4): S16-S23. [PDF Full-Text](#)

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Background In patients with heart failure (HF), assessment of functional capacity plays an important prognostic role. Both 6-minute walk and cardiopulmonary exercise testing have been used to determine physical function and to determine prognosis and even listing for transplantation. However, as in HF trials, the number of women reported has been small, and the cutoffs for transplantation have been representative of male populations and extrapolated to women. It is also well known that peak VO_2 as a determinant of fitness is inherently lower in women than in men and potentially much lower in the presence of HF. Values for a female population from which to draw for this important determination are lacking. **Methods** The HF-ACTION trial randomized 2,331 patients (28% women) with New York Heart Association class II-IV HF due to systolic dysfunction to either a formal exercise program in addition to optimal medical therapy or to optimal medical therapy alone without any formal exercise training. To characterize differences between men and women in the interpretation of final cardiopulmonary exercise testing models, the interaction of individual covariates with sex was investigated in the models of (1) VE/VCO_2 , (2) VO_2 at ventilatory threshold (VT), (3) distance on the 6-minute walk, and (4) peak VO_2 . **Results** The women were younger than the men and more likely to have a nonischemic etiology and a higher ejection fraction. Dose of angiotensin converting enzyme inhibitor (ACEI) was lower in the women, on average. The lower ACEI dose may reflect the higher use of angiotensin II receptor blocker (ARB) in women. Both the peak VO_2 and the 6-minute walk distance were significantly lower in the women than in the men. Perhaps the most significant finding in this dataset of baseline characteristics is that the peak VO_2 for

women was significantly lower than that for men with similar ventricular function and health status. Conclusion Therefore, in a well-medicated, stable, class II-IV HF cohort of patients who are able to exercise, women have statistically significantly lower peak VO₂ and 6-minute walk distance than men with similar health status and ventricular function. These data should prompt careful thought when considering prognostic markers for women and listing for cardiac transplant. (Am Heart J 2009;158:S16-S23.)

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Cardiology

Rastogi, S., M. S. Sabbah and H. N. Sabbah (2009). "Stromal Cell-Derived Factor-1, Fibroblast, and Vascular Endothelial Growth Factors Are Increased in Hypoxia-Conditioned Bone Marrow-Derived Stem Cell Medium." Circulation Research **105**(7): P8. [Article Request Form](#)

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Cardiology

Russell, S. D., M. A. Saval, J. L. Robbins, M. H. Ellestad, S. S. Gottlieb, E. M. Handberg, Y. Zhou and B. Chandler (2009). "New York Heart Association functional class predicts exercise parameters in the current era." American Heart Journal **158**(4): S24-S30. [PDF Full-Text](#)

[Russell, Stuart D.] Johns Hopkins Univ Hosp, Dept Med, Baltimore, MD 21287 USA. [Saval, Matthew A.] Henry Ford Hosp, Div Cardiol, Detroit, MI 48202 USA. [Robbins, Jennifer L.] Duke Univ, Med Ctr, Div Cardiol, Durham, NC 27710 USA. [Ellestad, Myrvin H.] Long Beach Mem Heart Inst, Long Beach Mem Heart & Vasc Inst, Long Beach, CA USA. [Gottlieb, Stephen S.] Univ Maryland, Sch Med, Div Cardiol, Baltimore, MD 21201 USA. [Handberg, Eileen M.] Univ Florida, Div Cardiol, Gainesville, FL USA. [Zhou, Yi] Duke Clin Res Inst, Durham, NC USA. [Chandler, Bleakley] Univ Hosp, Augusta, GA USA.

Russell, SD, Johns Hopkins Univ Hosp, Dept Med, 600 N Wolfe St, Carnegie 568, Baltimore, MD 21287 USA. srusse14@jhmi.edu

Background The New York Heart Association (NYHA) functional class is a subjective estimate of a patient's functional ability based on symptoms that do not always correlate with the objective estimate of functional capacity, peak oxygen consumption (peak VO₂). In addition, relationships between these 2 measurements have not been examined in the current medical era when patients are using beta-blockers, aldosterone antagonists, and cardiac resynchronization therapy (CRT). Using baseline data from the HF-ACTION (Heart Failure and A Controlled Trial Investigating Outcomes of Exercise TraiNing) study, we examined this relationship. **Methods** One thousand seven hundred fifty-eight patients underwent a symptom-limited metabolic stress test and stopped exercise due to dyspnea or fatigue. The relationship between NYHA functional class and peak VO₂ was examined. In addition, the effects of beta-blockers, aldosterone antagonists, and CRT therapy on these relationships were compared. **Results** The NYHA II patients have a significantly higher peak VO₂ (16.1 +/- 4.6 vs 13.0 +/- 4.2 mL/kg per minute), a lower ventilation (V_e)/VCO₂ slope (32.8 +/- 7.7 vs 36.8 +/- 10.4), and a longer duration of exercise (11.0 +/- 3.9 vs 8.0 +/- 3.4 minutes) than NYHA III/IV patients. Within each functional class, there was no difference in any of the exercise parameters between patients on or off of beta-blockers, aldosterone antagonists, or CRT therapy. Finally, with increasing age, a significant difference in peak VO₂, V_e/VCO₂ slope, and exercise time was found. **Conclusion** For patients being treated with current medical therapy, there still is a difference in true functional capacity between NYHA functional class II and III/IV patients. However, within each NYHA functional class, the presence or absence of contemporary heart failure therapies does not alter exercise parameters. (Am Heart J 2009; 158:S24-S30.)

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Cardiology

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." American Journal of Therapeutics **16**(5): 462-465. [PDF Full-Text](#)

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[Tucciarone, Michael; Dileo, Patricia Arizaca] Henry Ford Hosp, Dept Med, Detroit, MI 48202 USA. [Rodriguez Castro, Eduardo] Juan Maria de Salvatierra Hosp, Dept Med, La Paz, Baja California, Mexico.
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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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Cardiology

Whellan, D. J., S. J. Ellis, W. E. Kraus, K. Hawthorne, I. L. Pina, S. J. Keteyian, D. W. Kitzman, L. Cooper, K. Lee and C. M. O'Connor (2009). "Method for Establishing Authorship in a Multicenter Clinical Trial." Annals of Internal Medicine **151**(6): 414-20. [PDF Full-Text](#)

Duke Univ, Med Ctr, Durham, NC USA. Duke Clin Res Inst, Durham, NC USA. Wake Forest Univ, Sch Med, Winston Salem, NC USA. Massachusetts Gen Hosp, Boston, MA 02114 USA. Case Western Reserve Univ, Cleveland, OH 44106 USA. Henry Ford Hosp, Detroit, MI 48202 USA. NHLBI, NIH, Bethesda, MD 20892 USA. [Whellan, David J.] Jefferson Med Coll, Dept Cardiol, Philadelphia, PA 19107 USA.
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With the emergence of large multicenter trials over the past 20 years, the numbers of investigators involved and publications resulting from each study have grown exponentially. An efficient, fair, and effective way to establish authorship on study-related manuscripts could diminish conflict among the investigators and help ensure robust and timely dissemination of study results. This article describes a process developed by the investigators in the HF-ACTION (Heart Failure: A Controlled Trial Investigating Outcomes of Exercise Training) trial (ClinicalTrials.gov registration number: NCT00047437) to establish authorship of the manuscripts describing the baseline characteristics, study design, and trial outcomes in an equitable and transparent manner based on objective, quantifiable contributions to the study as a whole. The HF-ACTION investigators developed a scoring system that assigned points to investigators by using the criteria established for enrollment, adherence to the exercise program, data completion, committee service, and other trial efforts. The scoring system has been successfully implemented for baseline manuscripts and has allowed many investigators to participate in the HF-ACTION publication process.

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Dermatology

Gold, L. S., J. Tan, A. Cruz-Santana, K. Papp, Y. Poulin, J. Schlessinger, J. Gidner, Y. Liu, M. Graeber and B. P. O. S. G. Adapalene (2009). "A North American study of adapalene-benzoyl peroxide combination gel in the treatment of acne." Cutis **84**(2): 110-6. [PDF Full-Text](#) - ID=sladenjournals@hfhs.org PW=frank

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A fixed-dose combination gel with adapalene 0.1% and benzoyl peroxide (BPO) 2.5% recently has been developed for the treatment of acne vulgaris. In this multicenter, randomized, double-blind, parallel-group, active- and vehicle-controlled study conducted at 60 centers in the United States, Puerto Rico, and Canada, we assessed the efficacy and safety of adapalene-BPO combination gel in comparison with adapalene and BPO monotherapies as well as the gel vehicle. Participants with moderate facial acne vulgaris (rated 3 on the 5-point investigator global assessment of acne severity scale) were recruited and randomized to receive once-daily treatment with adapalene-BPO combination gel, adapalene monotherapy, BPO monotherapy, or gel vehicle for 12 weeks. They were assessed for success rate (the percentage of participants with investigator global assessment of acne severity rated clear or almost clear) and percentage change in inflammatory lesion (IL), noninflammatory lesion (NIL), and total lesion counts. Of the 1668 participants enrolled, 1429 (85.7%) completed the study. At study end point, adapalene-BPO combination gel showed a significantly higher success rate ($P < = .006$) and a greater percentage reduction in all acne lesion counts ($P < = .017$)

compared with the other treatment groups. A significant early treatment effect of adapalene-BPO combination gel at week 1 compared with adapalene monotherapy and vehicle also was observed for all lesion count reductions ($P < .001$). The safety of adapalene-BPO combination gel was comparable with adapalene and BPO monotherapies and vehicle. In a large clinical trial, the adapalene-BPO fixed-dose combination gel has shown superiority in efficacy compared with adapalene and BPO monotherapies and vehicle, with an early onset of efficacy and a good safety profile.

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Dermatology

Hoffman, D. M. and T. Shwayder (2009). "A crusted, friable papule on the scalp of a 17-month-old boy." *Pediatr Dermatol* **26**(5): 615-6. [PDF Full-Text](#)

Department of Dermatology, Henry Ford Hospital, Detroit, Michigan, USA.

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Dermatology

Sage, R. J., M. L. Chaffins and D. J. Kouba (2009). "Granulomatous Foreign Body Reaction to Hyaluronic Acid: Report of a Case After Melolabial Fold Augmentation and Review of Management." *Dermatologic Surgery* **35**(2): 1696-1700. [PDF Full-Text](#)

[Kouba, David J.] Henry Ford Hlth Syst, Div Mohs Microg Surg, Detroit, MI USA. [Chaffins, Marsha L.] Henry Ford Hlth Syst, Div Dermatopathol, Detroit, MI USA.

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Dermatology

Tierney, E. P., D. J. Kouba and C. W. Hanke (2009). "Review of Fractional Photothermolysis: Treatment Indications and Efficacy." *Dermatologic Surgery* **35**(10): 1445-1461. [PDF Full-Text](#)

[Tierney, Emily P.; Hanke, C. William] St Vincents Hosp, Laser & Skin Surg Ctr Indiana, Carmel, IN 46032 USA. [Kouba, David J.] Henry Ford Hlth Syst, Dept Dermatol, Div Mohs Microg Surg, Detroit, MI USA.

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BACKGROUND Fractional photothermolysis (FP) is one of the most significant milestones in laser technology and resurfacing. **METHODS** Review of the Medline English literature and recent international conferences regarding FP technology, applications, and indications. **RESULTS** Successful conditions treated with nonablative FP reported in the literature include acne scarring; dyschromia and fine wrinkling of photoaging on the face, chest, neck, and hands; melasma; poikiloderma of Civatte; nevus of Ota; scars; minocycline hyperpigmentation; telangiectatic matting; residual hemangioma; granuloma annulare; colloid milium; and disseminated superficial actinic porokeratosis. An advance in 2007 was the introduction of ablative FP (AFP), which results in significantly greater improvement in skin laxity and textural abnormalities. Most recently, AFP has demonstrated significantly greater improvement than nonablative FP in reducing acne scarring and skin redundancy and laxity associated with photoaging. **CONCLUSIONS** Through the induction of microthermal zones of injury, FP technology stimulates a robust and rapid wound healing response resulting in improvement in a diversity of aesthetic, inflammatory, and preneoplastic skin disorders. Further investigation into the technology and diverse array of cutaneous conditions that can benefit from FP is highly needed. The authors have indicated no significant interest with commercial supporters.

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Diagnostic Radiology

Ali, M. M., G. Liu, T. Shah, C. A. Flask and M. D. Pagel (2009). "Using two chemical exchange saturation transfer magnetic resonance imaging contrast agents for molecular imaging studies." *Acc Chem Res* **42**(7): 915-24. [Article Request Form](#)

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

Responsive magnetic resonance imaging (MRI) contrast agents can change MR image contrast in response to a molecular biomarker. Quantitative detection of the biomarker requires an accounting of the other effects that may alter MR image contrast, such as a change in the agent's concentration, magnetic field variations, and hardware sensitivity profiles. A second unresponsive MRI contrast agent may serve as an "internal control" to isolate the detection of the molecular biomarker. Chemical exchange saturation transfer (CEST) MRI contrast agents can be selectively detected, providing the opportunity to combine a responsive CEST agent and an unresponsive CEST agent during the same MRI scan session. When two CEST MRI contrast agents are used for molecular imaging applications, the CEST agents should be designed to maximize accurate quantification of the concentrations of the two agents. From a chemical perspective, CEST agents behave like enzymes that catalyze the conversion of an unsaturated water "substrate" into a saturated water "product". The analysis of CEST agent kinetics parallels the Michaelis-Menten analysis of enzyme kinetics, which can be used to correlate the CEST effect with the concentration of the agent in solution. If the concentration of water "substrate" that is available to the CEST agent is unknown, which may be likely for in vivo MRI studies, then only a ratio of concentrations of the two CEST agents can be measured. In both cases, CEST agents should be designed with minimal T(1) relaxivity to improve concentration quantifications. CEST agents can also be designed to maximize sensitivity. This may be accomplished by incorporating many CEST agents within nanoparticles to create a large number of exchangeable protons per nanoparticle. Finally, CEST agents can be designed with rapid detection in mind. This may be accomplished by minimizing T(1) relaxivity of the CEST agent so that MRI acquisition methods have time to collect many MRI signals following a single selective saturation period. In this Account, we provide an example that shows the sensitive and rapid detection of two CEST agents in an in vivo MRI study of a mouse model of mammary carcinoma. The ratio of the concentrations of the two CEST agents was quantified with analysis methods that parallel Michaelis-Menten enzyme kinetic analysis. This example demonstrates current limitations of the method that require additional research, but it also shows that two CEST MRI contrast agents can be detected and quantitatively assessed during in vivo molecular imaging studies.

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Diagnostic Radiology

Ali, M. M., B. Yoo and M. D. Pagel (2009). "Tracking the Relative In Vivo Pharmacokinetics of Nanoparticles with PARACEST MRI." Molecular Pharmaceutics 6(5): 1409-1416. [Article Request Form](#)

[Pagel, Mark D.] Univ Arizona, Arizona Canc Ctr, Biomed Engr Interdisciplinary Program, Tucson, AZ 85724 USA. [Pagel, Mark D.] Univ Arizona, Dept Chem, Tucson, AZ 85724 USA. [Ali, M. Meser] Henry Ford Hlth Syst, Dept Radiol, Detroit, MI USA.

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A noninvasive assay that tracks the relative in vivo pharmacokinetics of two nanoparticles may accelerate the development of nanoparticles for biomedical applications, and may provide a method to select personalized nanomedicines for individual patients. To develop an in vivo competitive assay, two MRI contrast agents that could be selectively detected through paramagnetic chemical exchange saturation transfer (PARACEST) were conjugated to a second generation and fifth generation polyamidoamine (PAMAM) dendrimer. The CEST effects of each agent was calibrated relative to concentration. The effects of T-1 relaxivities of these dendritic PARACEST magnetic resonance imaging (MRI) contrast agents were found to be negligible relative to their CEST effects with respect to changes in image contrast, which facilitated the measurement of the ratios of their chemical exchange lifetimes. Injection of both contrast agents into a mouse model of mammary carcinoma resulted in a temporal increase in the CEST effect from each agent in the flank tumor. Although the in vivo CEST effects could not be used to determine the absolute concentrations of each agent within the tumor, the ratio of the in vivo CEST effects was used to measure the ratio of the concentrations of the agents. This result demonstrated that the relative in vivo pharmacokinetics of two nanoparticles may be evaluated using PARACEST MRI.

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Diagnostic Radiology

Al-Mallah, M. and R. Y. Kwong (2009). "Clinical Application of Cardiac CMR." Reviews in Cardiovascular Medicine **10**(3): 134-141. [Article Request Form](#)

[Al-Mallah, Mouaz] Wayne State Univ, Sch Med, Detroit, MI 48202 USA. [Al-Mallah, Mouaz] Henry Ford Hosp, Adv Cardiovasc Imaging, Detroit, MI 48202 USA. [Kwong, Raymond Y.] Brigham & Womens Hosp, Div Cardiovasc, Boston, MA 02115 USA.

Al-Mallah, M, Wayne State Univ, Sch Med, Detroit, MI 48202 USA.

Cardiovascular magnetic resonance (CMR) imaging is an important clinical tool that aids in the diagnosis and management of patients with cardiomyopathy. With its ability to assess morphologic and physiologic myocardial characteristics in the same imaging session, CMR can effectively rule out less common causes of cardiomyopathy, including cardiac hemochromatosis, amyloidosis, and arrhythmogenic right ventricular tachycardia. The combination of cine function, myocardial perfusion at rest and under stress, and late gadolinium enhancement provides a strong assessment that can establish the cause of the cardiomyopathy as well as guide therapy in cases of ischemic cardiomyopathy. CMR can also identify microvascular obstruction in acute myocardial infarction. This technique can be especially helpful in the diagnosis of conditions such as arrhythmogenic right ventricular dysplasia, cardiac sarcoidosis, and myocarditis. It can also be used to evaluate patients with chest pain and pericardial diseases. [Rev Cardiovasc Med. 2009;10(3):134-141 doi: 10.3909/ricm0463] (C) 2009 MedReviews (R), LLC

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Diagnostic Radiology

Jain, R., S. Ellika, N. L. Lehman, L. Scarpace, L. R. Schultz, J. P. Rock, M. Rosenblum and T. Mikkelsen (2009). "Can permeability measurements add to blood volume measurements in differentiating tumefactive demyelinating lesions from high grade gliomas using perfusion CT?" J Neurooncol **EPub Ahead of Print**. [PDF Full-Text](#)

Division of Neuroradiology, Department of Radiology, Henry Ford Health System, 2799 West Grand Blvd, Detroit, MI, 48202, USA, rajanj@rad.hfh.edu

Tumefactive demyelinating lesions (TDLs) can mimic a neoplasm on conventional imaging and may necessitate biopsy for diagnosis. The purpose of this study was to differentiate TDLs from high grade gliomas based on physiologic (permeability) and hemodynamic (blood volume) parameters using perfusion CT. Five patients who presented with tumefactive enhancing lesions on initial MRI that mimicked a neoplasm underwent perfusion CT. We compared the perfusion CT parameters of these patients with those of 24 patients with high grade gliomas. TDLs showed lower permeability surface area product (PS) (0.8 +/- 0.2 vs 2.4 +/- 1.4 ml/100 g/min, P-value 0.014) and lower cerebral blood volume (CBV) (1.0 +/- 0.2 vs 2.8 +/- 1.2 ml/100 g, P-value 0.006) as compared to high grade gliomas. TDLs show lower PS and CBV as compared to high grade gliomas, to which they can mimic on conventional MR imaging, due to lack of neoangiogenesis and vascular endothelial proliferation and hence perfusion CT can be used to differentiate the two entities.

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Emergency Medicine

Paxton, J. H., T. E. Knuth and H. A. Klausner (2009). "Proximal humerus intraosseous infusion: a preferred emergency venous access." J Trauma **67**(3): 606-11. [PDF Full-Text](#)

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PURPOSE: To assess the proximal humerus intraosseous (PHIO) catheter placement as a preferred method for venous access over conventional methods, including peripheral intravenous (PIV) and central venous catheters (CVCs), during emergency room resuscitation. **METHODS:** In phase 1, conventional methods for venous access (PIV and CVC) were assessed for all patients presenting to the emergency department resuscitation bay. Outcome measures in both phases were speed, immediate complications, and pain. CVC placement was performed when PIV access was deemed impossible or when rapid volume resuscitation was needed. In phase 2, resuscitations requiring venous access or complicated by failed PIV access attempts underwent PHIO catheter placement. **RESULTS:** Sixty-two patients received either PIV (57) or CVC (5) catheterization, and 29 patients received 30 PHIO catheters. PHIO catheter placement was significantly faster than conventional methods (1.5 [SD 1.1] versus 3.6 minutes [SD 3.7; p < 0.001 for PIV, and 15.6 minutes [SD 6.7; p < 0.0056] for CVC). No major complications were identified in either phase. Minor complications for PIV

access included extravasation and placement failure. Minor complications for CVC placement included inability to thread the guidewire. Minor complications with PHIO catheter placement included placement failure, poor flow, and catheter dislodgement. Pain scores associated with PHIO insertion and infusion were higher than those associated with PIV and CVC catheter placement. CONCLUSION: PHIO catheter placement is significantly faster than PIV and CVC placement with increased minor complication profile and perceived pain. PHIO venous access is absolutely life saving when PIV or CVC placement is difficult or impossible.

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Emergency Medicine

Tsalik, E. L., D. Jones, B. Nicholson, L. Waring, O. Liesenfeld, L. P. Park, S. W. Glickman, L. B. Caram, R. J. Langley, J. C. van Velkinburgh, C. B. Cairns, E. P. Rivers, R. M. Otero, S. F. Kingsmore, T. Lalani, V. G. Fowler and C. W. Woods (2009). "Multiplex PCR to Diagnose Blood Stream Infections in Patients Admitted from the Emergency Department with Sepsis." J Clin Microbiol **Epub Ahead of Print**. [Article Request Form](#)

From the Department of Medicine, Division of Infectious Diseases (ELT, LPP, LBC, VGF, CWW), Duke University School of Medicine, Durham, North Carolina; (DJ, BN) Department of Medicine Durham VA Medical Center, Durham, North Carolina; (SWG, CBC, LTG) Department of Emergency Medicine, University of North Carolina School of Medicine, Chapel Hill, NC; (RMO, EPR) Henry Ford Hospital, Wayne State University, Detroit MI; (RJL, JCV, SFK) The National Center for Genome Resources, Santa Fe, NM; (LW, OL) Roche Molecular Diagnostics; (TL) Naval Medical Center Portsmouth, Portsmouth, VA.

Background: Sepsis represents a heterogeneous group of infectious etiologies. Early diagnosis and provision of appropriate antimicrobial therapy correlates with positive clinical outcomes. Current microbiological techniques are limited in diagnostic capacity and timeliness. Multiplex PCR has the potential to rapidly identify blood stream infections and fill this diagnostic gap. Methods: We identified patients from a large academic hospital emergency department with suspected sepsis. A Multiplex PCR that can detect 25 bacterial and fungal pathogens was compared to blood culture. Results were analyzed with respect to likelihood of infection, sepsis severity, site of infection, and the effect of prior antibiotic therapy. Results: We enrolled 306 subjects with suspected sepsis. Of these, 43 were later determined not to have infectious etiologies. Of the remaining 263 subjects, 70% had sepsis, 16% had severe sepsis and 14% had septic shock. The majority had definite (41.5%) or probable infection (30.7%). Blood culture and PCR performed similarly among patients with clinically defined infection (AUC 0.64 vs. 0.60, respectively). However, blood culture identified more cases of septicemia than did PCR among patients with an identified infectious etiology (66 vs. 46; $p=0.0004$). The two tests performed similarly when stratified by sepsis severity or infection site. Blood culture tended to detect infections more frequently among patients who received prior antibiotics ($p=0.06$). Conversely, PCR identified an additional 24 organisms that blood culture failed to detect. Conclusions: Real-time multiplex PCR has the potential to serve as an adjunct to conventional blood culture, adding diagnostic yield and shortening the time to pathogen identification.

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Gastroenterology

Feng, Z. Z., J. Tang, D. Y. Kim, K. Brown, M. Abouljoud, S. Gordon, A. Yoshida, M. A. Huang, G. Divine and D. K. Moonka (2009). "Renal insufficiency after liver transplantation in the MELD era compared to the pre-MELD era." Clinical Transplantation **23**(5): 637-642.

[PDF Full-Text](#)

[Feng, Zhen-Zhou; Tang, Jeffrey; Brown, Kimberly; Gordon, Stuart; Huang, Mary Ann; Moonka, Dilip Kumar] Henry Ford Hlth Syst, Div Gastroenterol, Detroit, MI 48202 USA. [Kim, Dean Y.; Abouljoud, Marwan; Yoshida, Atsushi] Henry Ford Hlth Syst, Dept Transplant Surg, Detroit, MI 48202 USA. [Divine, George] Henry Ford Hlth Syst, Dept Biostat, Detroit, MI 48202 USA.

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Because the model for end-stage liver disease (MELD) system for liver allocation gives priority to patients with a higher creatinine, and because pre-transplant renal function is one determinant of post-transplant renal function, this study compares the burden of renal insufficiency in the pre-MELD and MELD eras. Two hundred and eleven patients, at our institution, transplanted in the pre-MELD era, were compared to 143 in the MELD era. The GFR (mL/min/1.73 m²) was significantly higher in the MELD cohort than the pre-MELD cohort at time

of transplant, discharge, and 12 months post-transplant (95.5 vs. 85.3, $p = 0.039$; 90.4 vs. 77.4, $p = 0.002$; 66.8 vs. 60.3, $p = 0.026$). There was no difference between the two groups in time to renal failure. There was a higher rate of sirolimus use in the MELD era (27% vs. 18%; $p = 0.042$) and a slightly higher use of kidney-liver transplant in the MELD era ($p = 0.056$). We did not identify greater renal insufficiency in the MELD era. There was greater renal function in the MELD era at time of transplant, discharge and month 12. Potential explanations include: absence of an increase in renal insufficiency prior to transplant in the MELD era, greater use of renal sparing immunotherapy and growing use of kidney-liver transplant.

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Gastroenterology

Krishnan, P. V., Z. Z. Feng and S. C. Gordon (2009). "Prolonged intrahepatic cholestasis and renal failure secondary to anabolic androgenic steroid-enriched dietary supplements." J Clin Gastroenterol **43**(7): 672-5. [PDF Full-Text](#)

Division of Gastroenterology and Hepatology, Henry Ford Hospital, Detroit, MI, 48202, USA.

The illegal enrichment of anabolic androgenic steroids in over-the-counter dietary supplements is well documented, but the health consequences have not been widely recognized. Three recent reports document cholestatic jaundice and nephropathy due to these compounds. We present 3 additional cases of anabolic androgenic steroid-enriched dietary supplement-induced hepatotoxicity and 1 case of renal failure, and we review the literature and the relevant features of this growing health concern. Recognition of this entity could obviate the need for invasive diagnostic testing and hospitalization and facilitate diagnosis and appropriate counseling.

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Health Enhancement Center

Horwich, T. B., E. S. Leifer, C. A. Brawner, M. B. Fitz-Gerald and G. C. Fonarow (2009). "The relationship between body mass index and cardiopulmonary exercise testing in chronic systolic heart failure." American Heart Journal **158**(4): S31-S36. [PDF Full-Text](#)

[Fonarow, Gregg C.] Ronald Reagan UCLA Med Ctr, Ahmanson UCLA Cardiomyopathy Ctr, Los Angeles, CA 90095 USA. [Leifer, Eric S.] NHLBI, Bethesda, MD 20892 USA. [Brawner, Clinton A.] Henry Ford Hosp, Detroit, MI 48202 USA. [Fitz-Gerald, Meredith B.] Univ Alabama, Birmingham, AL USA. Fonarow, GC, Ronald Reagan UCLA Med Ctr, Ahmanson UCLA Cardiomyopathy Ctr, 10833 LeConte Ave, Room 47-123 CHS, Los Angeles, CA 90095 USA. gfonarow@mednet.ucla.edu

Background Cardiopulmonary exercise testing (CPX) in patients with systolic heart failure (HF) is important for determining HF prognosis and helping guide timing of heart transplantation. Although approximately 20% to 30% of patients with HF are obese (body mass index [BMI] >30 kg/m²), the impact of BMI on CPX results is not well established. The objective of this study was to assess the relationship between BMI and CPX variables, including peak oxygen uptake (VO₂) at ventilatory threshold, oxygen pulse, and ventilation-carbon dioxide production ratio. Methods Consecutive patients with systolic HF ($n = 2,324$) enrolled in the Heart Failure and A Controlled Trial Investigating Outcomes of Exercise Training trial who had baseline BMI recorded were included in this study. Subjects were divided into strata based on BMI: underweight (BMI <18.5 kg/m²), normal weight (BMI 18.5-24.9 kg/m²), overweight (BMI 25.0-29.9 kg/m²), obese I (BMI 30-34.9 kg/m²), obese II (BMI 35-39.9 kg/m²), and obese III (BMI ≥ 40 kg/m²). Results Obese III, but not overweight; obese I; or obese II was associated with decreased peak VO₂ (mL kg⁻¹ min⁻¹) compared to normal weight status. Increasing BMI category was inversely related to ventilation/carbon dioxide production (V-E/V-CO₂) ratio ($P < .0001$). On multivariable analysis, BMI was a significant independent predictor of peak VO₂ (partial R² = 0.07, $P < .0001$) and V-E/V-CO₂ slope (partial R² = 0.03, $P < .0001$) in patients with chronic systolic HF. Conclusions Body mass index is significantly associated with key CPX fitness variables in patients with HF. The influence of BMI on the prognostic value of CPX in HF requires further evaluation in longitudinal studies. (Am HeartJ 2009J 58:S31-S36.)

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Hematology, Medical Oncology & Josephine Ford Cancer Center

Zuberi, L., D. Yerasuri and P. Kuriakose (2009). "Effect of blood group on idiopathic thrombotic thrombocytopenic purpura." J Clin Apher **24**(4): 131-3. [PDF Full-Text](#)

Thrombotic thrombocytopenic purpura (TTP) is a condition caused by deficiency of ADAMTS13 resulting in accumulation of ultra large Von Willebrand factor multimers (ULVWF), leading to micro thrombi in multiple organs. The varying susceptibilities of blood group antigens to ADAMTS13 have been demonstrated. A and B antigens are protective of VWF; and VWF purified from blood group O individuals has been shown to be cleaved faster by ADAMTS13 compared to VWF from blood group AB individuals. We proposed that there may be a difference in the incidence of blood groups in TTP patients compared with the general population. We felt this to be important for a life-threatening disease with poorly understood epidemiology. We report a retrospective analysis of 74 patients presenting from 1993 to 2008 with idiopathic TTP. We studied the incidence across various blood groups and also estimated the recurrence and mortality in each group. The incidence of various blood groups were as follows: O 36%, A 36%, B 25%, and AB 2%, compared with expected frequencies in the Detroit area: O 44%, A 33% B 20%, and AB 3%. There was a trend of lower than expected frequency of blood group O. There were 24 recurrences and 14 deaths, uniform across blood groups. We hypothesized that there may be an association between blood groups and the risk of TTP; however the differences in our study were not statistically significant. Recurrence and disease specific mortality did not appear to be impacted by blood group.

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Hypertension & Vascular Research

Atchison, D. K. and W. H. Beierwaltes (2009). "Inhibition of NaCl Reabsorption with Furosemide Decreases Renal Cortical Interstitial Calcium While Stimulating Plasma Renin Activity." Hypertension **54**(4): E115-E116. [PDF Full-Text](#) - Scroll down to the bottom of the Table of Contents

[Atchison, Douglas K.; Beierwaltes, William H.] Henry Ford Hosp, Detroit, MI 48202 USA.

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Hypertension & Vascular Research

Haque, M. Z. and P. A. Ortiz (2009). "High Salt Differentially Regulates Surface NKCC2 in Thick Ascending Limbs of Dahl Salt-Sensitive and Salt-Resistant Rats." Hypertension **54**(4): E34-E35. [PDF Full-Text](#) - Scroll down to the bottom of the Table of Contents

[Haque, Mohammed Z.; Ortiz, Pablo A.] Henry Ford Hosp, Detroit, MI 48202 USA.

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Hypertension & Vascular Research

He, Q., P. Harding and M. C. LaPointe (2009). "Rap, PKA, ERK1/2, and p90RSK are Involved in EP4-Dependent PGE(2) Signaling in Neonatal Ventricular Myocytes." Hypertension **54**(4): E54-E54. [PDF Full-Text](#) - Scroll down to the bottom of the Table of Contents

[He, Quan; Harding, Pamela; LaPointe, Margot C.] Henry Ford Hosp, Detroit, MI 48202 USA.

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Hypertension & Vascular Research

Herrera, M. and J. L. Garvin (2009). "Angiotensin II Stimulates Thick Ascending Limb NO Production by Activating the AT2 Receptors." Hypertension **54**(4): E34-E34. [PDF Full-Text](#) - Scroll down to the bottom of the Table of Contents

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Hypertension & Vascular Research

Kim, Y. H., T. D. Pham, W. Zheng, S. Hong, C. Baylis, V. Pech, W. H. Beierwaltes, D. B. Farley, L. E. Braverman, J. W. Verlander and S. M. Wall (2009). "Role of pendrin in iodide balance: going with the flow." *American Journal of Physiology-Renal Physiology* **297**(4): F1069-F1079. [PDF Full-Text](#)

[Wall, Susan M.] Emory Univ, Sch Med, Div Renal, Dept Med, Atlanta, GA 30322 USA. [Wall, Susan M.] Emory Univ, Sch Med, Dept Physiol, Atlanta, GA 30322 USA. [Zheng, Wencui; Baylis, Christine; Verlander, Jill W.] Univ Florida, Dept Med, Gainesville, FL USA. [Beierwaltes, William H.] Henry Ford Hosp, Dept Internal Med, Hypertens & Vasc Res Div, Detroit, MI 48202 USA. [Braverman, Lewis E.] Boston Univ, Sch Med, Dept Med, Boston, MA 02118 USA. [Farley, Donna B.] Univ Iowa, Dept Med, Iowa City, IA 52242 USA. Wall, SM, Emory Univ, Sch Med, Div Renal, Dept Med, WMB Rm 338,1639 Pierce Dr, Atlanta, GA 30322 USA. smwall@emory.edu

Kim YH, Pham TD, Zheng W, Hong S, Baylis C, Pech V, Beierwaltes WH, Farley DB, Braverman LE, Verlander JW, Wall SM. Role of pendrin in iodide balance: going with the flow. *Am J Physiol Renal Physiol* 297: F1069-F1079, 2009. First published July 15, 2009; doi:10.1152/ajprenal.90581.2008.-Pendrin is expressed in the apical regions of type B and non-A, non-B intercalated cells, where it mediates Cl⁻ absorption and HCO₃⁻ secretion through apical Cl⁻/HCO₃⁻ exchange. Since pendrin is a robust I⁻ transporter, we asked whether pendrin is upregulated with dietary I⁻ restriction and whether it modulates I⁻ balance. Thus I⁻ balance was determined in pendrin null and in wild-type mice. Pendrin abundance was evaluated with immunoblots, immunohistochemistry, and immunogold cytochemistry with morphometric analysis. While pendrin abundance was unchanged when dietary I⁻ intake was varied over the physiological range, I⁻ balance differed in pendrin null and in wild-type mice. Serum I⁻ was lower, while I⁻ excretion was higher in pendrin null relative to wild-type mice, consistent with a role of pendrin in renal I⁻ absorption. Increased H₂O intake enhanced differences between wild-type and pendrin null mice in I⁻ balance, suggesting that H₂O intake modulates pendrin abundance. Raising water intake from similar to 4 to similar to 11 ml/day increased the ratio of B cell apical plasma membrane to cytoplasm pendrin label by 75%, although circulating renin, aldosterone, and serum osmolality were unchanged. Further studies asked whether H₂O intake modulates pendrin through the action of AVP. We observed that H₂O intake modulated pendrin abundance even when circulating vasopressin levels were clamped. We conclude that H₂O intake modulates pendrin abundance, although not likely through a direct, type 2 vasopressin receptor-dependent mechanism. As water intake rises, pendrin becomes increasingly critical in the maintenance of Cl⁻ and I⁻ balance.

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[Li, Xiao C.; Zhang, Fan; Zhuo, Jia L.] Henry Ford Hosp, Detroit, MI 48202 USA. [Cook, Julie L.] Ochsner Clin Fdn, New Orleans, LA USA. [Rubera, Isabelle; Tauc, Michel] Univ Nice Sophia Antipolis, Parc Valrose, France.

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Hypertension & Vascular Research

Liao, T. D., X. P. Yang, N. E. Rhaleb and O. A. Carretero (2009). "N-Acetyl-Seryl-Aspartyl-Lysyl-Proline Regresses Renal Dysfunction, Inflammation, and Fibrosis in Rats with 5/6 Nephrectomy-Induced Hypertension." *Hypertension* **54**(4): E86-E86. [PDF Full-Text](#) - Scroll down to the bottom of the Table of Contents

[Liao, Tang-Dong; Yang, Xiao-Ping; Rhaleb, Nour-Eddine; Carretero, Oscar A.] Henry Ford Hosp, Detroit, MI 48202 USA.

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Ortiz, P. A. (2009). "Toll-like receptor 4 (TLR-4) regulates renal ion transport." [American Journal of Physiology-Renal Physiology](#) **297**(4): F864-F865. [PDF Full-Text](#)

[Ortiz, Pablo A.] Wayne State Univ, Henry Ford Hosp, Dept Internal Med, Hypertens & Vasc Res Div, Detroit, MI 48202 USA. [Ortiz, Pablo A.] Wayne State Univ, Dept Physiol, Detroit, MI 48202 USA.
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Hypertension & Vascular Research

Peng, H. M., O. A. Carretero, X. P. Yang, J. Xu, Y. H. Liu, M. D'Ambrosio, P. Leung and N. E. Rhaleb (2009). "Effects of Angiotension II-Induced Hypertension on the Heart in Mice with Th1/Th2 Profiles." [Hypertension](#) **54**(4): E76-E77. [PDF Full-Text](#) - Scroll down to the bottom of the Table of Contents

[Peng, Hongmei; Carretero, Oscar A.; Yang, Xiao-Ping; Xu, Jiang; Liu, Yun-He; D'Ambrosio, Martin; Leung, Pablo; Rhaleb, Nour-Eddine] Henry Ford Hosp, Detroit, MI 48202 USA.

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[Ren, Yilin; Garvin, Jeffrey L.; D'Ambrosio, Martin A.; Wang, Hong; Carretero, Oscar A.] Henry Ford Hosp, Detroit, MI 48202 USA.

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Hypertension & Vascular Research

Silva, G. B. and J. L. Garvin (2009). "Extracellular ATP Inhibits Transport-Related Oxygen Consumption by the Thick Ascending Limb via Increasing NO." [Hypertension](#) **54**(4): E116-E116. [PDF Full-Text](#) - Scroll down to the bottom of the Table of Contents

[Silva, Guillermo B.; Garvin, Jeffrey L.] Henry Ford Hosp, Detroit, MI 48202 USA.

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Hypertension & Vascular Research

Silva, G. B. and J. L. Garvin (2009). "Akt1 mediates purinergic-dependent NOS3 activation in thick ascending limbs." [American Journal of Physiology-Renal Physiology](#) **297**(3): F646-F652. [PDF Full-Text](#)

[Silva, Guillermo B.; Garvin, Jeffrey L.] Henry Ford Hosp, Div Hypertens & Vasc Res, Detroit, MI 48202 USA.
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Silva GB, Garvin JL. Akt1 mediates purinergic-dependent NOS3 activation in thick ascending limbs. *Am J Physiol Renal Physiol* 297: F646-F652, 2009. First published July 1, 2009; doi:10.1152/ajprenal.00270.2009.- Extracellular ATP regulates many physiological processes via release of nitric oxide (NO). ATP stimulates NO in thick ascending limbs (TALs), but the signaling cascade involved in the cells of this nephron segment, as well as many other types of cells, is poorly understood. We hypothesized that ATP enhances NO synthase (NOS) activity by stimulating PI3 kinase and Akt. We measured 1) NO in TALs using the NO-sensitive dye DAF-2 DA and 2) Akt activity by fluorescence resonance energy transfer and phosphorylation of Akt isoforms. ATP (100 μ M) stimulated NO in wild-type mice [26 \pm 4 arbitrary units (AU)], but not in NOS3(-/-) mice (2 \pm 2 AU; P < 0.04). In the presence of the NOS1- and NOS2-selective inhibitors 7-NI and 1400W, ATP stimulated NO by 30 \pm 2 and 33 \pm 3 AU, respectively (not significant vs. control). In the presence of the PI3 kinase

inhibitor LY294002, ATP-increased NO was reduced by 85% (5 +/- 2 vs. 28 +/- 4 AU; P < 0.02). ATP alone increased Akt activity and this effect was significantly blocked by suramin, a P2 receptor antagonist. In the presence of an Akt-selective inhibitor, ATP-induced NO was blocked by 90 +/- 4%. ATP significantly stimulated Akt1 phosphorylation at Ser(473) by 91 +/- 13%, whereas Akt2 phosphorylation remained unchanged and Akt3 phosphorylation decreased. In vivo transduction of TALs with a dominant-negative Akt1 significantly decreased ATP-induced NO by 88 +/- 6%. We concluded that ATP increases NOS3-derived NO via Akt1 activation in the TAL.

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Hypertension & Vascular Research

Wang, F. F., Q. He, Y. Sun and X. P. Yang (2009). "Female Adult Cardiomyocytes are Protected Against Oxidative Stress." Hypertension **54**(4): E43-E43. [PDF Full-Text](#)
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[Wang, Fangfei; He, Quan; Sun, Ying; Yang, Xiao-ping] Henry Ford Hlth Syst, Detroit, MI USA.

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Hypertension & Vascular Research

Zhu, L. P., O. Carretero, P. Harding, H. W. Li, C. Sumners and X. P. Yang (2009). "Overexpression of Angiotensin II Type 2 Receptor Stimulates Bradykinin Release via Prolylcarboxypeptidase in Mouse Coronary Artery Endothelial Cells." Hypertension **54**(4): E72-E72. [Article Request Form](#)

[Zhu, Liping; Carretero, Oscar; Harding, Pamela; Yang, Xiao-Ping] Henry Ford Hlth Syst, Detroit, MI USA. [Li, Hongwei; Sumners, Colin] Univ Florida, Gainesville, FL USA.

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Infectious Diseases

Arabi, Z. and A. Boxwalla (2009). "Repeated Stool Toxin Testing for Diagnosing Difficile Colitis Is Still Valid." Southern Medical Journal **102**(10): 993-994. [PDF Full-Text](#)

[Arabi, Ziad] Henry Ford Hosp, Dept Internal Med, Detroit, MI 48202 USA. Henry Ford Hosp, Dept Infect Dis, Detroit, MI 48202 USA.

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Infectious Diseases

Nagappan, V., D. Boikov and J. A. Vazquez (2009). "Assessment of the In-vitro Kinetic Activity of Caspofungin against *Candida glabrata*." Antimicrob Agents Chemother **EPub Ahead of Print**. [Article Request Form](#)

Oakwood Hospital, Dearborn, MI; Henry Ford Hospital, Detroit, MI; Wayne State University School of Medicine, Detroit, MI.

Echinocandins have become the drug of choice in infections due to *Candida glabrata*. The objective was to evaluate the in vitro activity of caspofungin alone and in combination against *C. glabrata*. In vitro assays demonstrated that caspofungin alone showed excellent fungicidal activity against *C. glabrata*, including fluconazole-resistant strains. The combination of caspofungin/azoles showed potential synergy against *C. glabrata*. Overall, caspofungin demonstrated excellent in vitro activity alone and in combination against strains of *C. glabrata*.

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Infectious Diseases

Reyes, M. P., A. Ali, R. E. Mendes and D. J. Biedenbach (2009). "Resurgence of *Pseudomonas* Endocarditis in Detroit, 2006-2008." Medicine **88**(5): 294-301. [PDF Full-Text](#)

[Reyes, Milagros P.] Wayne State Univ, Harper Univ Hosp, Div Infect Dis, Dept Med, Detroit, MI 48201 USA.
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A resurgence of endocarditis due to *Pseudomonas aeruginosa* was seen in 10 injection drug users (IDUs) in Detroit between 2006 and 2008 (6 men, 4 women; mean age, 48.1 yr). All patients tested negative for the human immunodeficiency virus (HIV). Five patients had left-sided endocarditis of the mitral valve and/or the aortic valve; 3 of 5 patients had prosthetic valve endocarditis. Four of 10 patients had right-sided endocarditis of the tricuspid valve alone. One patient had bilateral involvement of the aortic and tricuspid valves. Nine patients had *Pseudomonas* endocarditis (PsE); 1 patient had mixed endocarditis with *P. aeruginosa* and *Candida parapsilosis*. Seven of 10 patients were treated with a combination of intravenous cefepime, 4-6 g/d, plus high-dose tobramycin (HDT) for at least 6 weeks. Tobramycin, 8 mg/kg per day, was given as a single daily dose intravenously, aiming for peak serum levels of 18-22 $\mu\text{g/mL}$ and trough levels of $< 11 \mu\text{g/mL}$. The patient with mixed endocarditis was also treated with fluconazole. Two patients initially treated with other antipseudomonal regimens, including cefepime alone and piperacillin/tazobactam plus tobramycin, failed treatment and were switched to cefepime and HDT. A third patient was switched to cefepime and ciprofloxacin because of nephrotoxicity. Two patients developed nephrotoxicity to tobramycin; 1 patient developed ototoxicity. The overall medical cure rate for both left-sided and right-sided disease was 80% (4/5). All 5 patients who required surgery survived (5/5; 100%). Overall outcome was 90% (9/10). Indications for valve replacement were recurrent *Pseudomonas* bacteremia ($n = 3$), recurrent bacteremia and congestive heart failure ($n = 1$), and persistent bacteremia and fungemia ($n = 1$). Tricuspid valvectomy with valve replacement was successful in 2 patients and in a third patient who had successful replacement of both the tricuspid and the aortic valve, for recurrent bacteremia and congestive heart failure. Two patients with pure left-sided prosthetic valve endocarditis underwent successful repeat valve replacements. Although this is a small series, the overall mortality rate (1/10; 10%) was low. The patient who did not survive had left-sided involvement of the aortic valve and could not undergo surgery because of a large embolic cerebral infarct. The mortality rate of left-sided disease in the current series was 16.7% (1/6 including the patient with tricuspid and aortic valve PsE) compared to 60% in a series of 15 patients reported in 1990. Our current antimicrobial regimen for PsE consists of a combination of cefepime, 6 g/d, in 3 divided doses, plus HDT, 8 mg/kg per day, given as a single daily dose for 6 weeks. For cefepime-resistant *Pseudomonas*, imipenem, 4-6 g/d, or meropenem, 6 g/d, plus HDT has been successful. For right-sided disease refractory to medical therapy, surgical intervention is recommended if *Pseudomonas* bacteremia persists for 2 weeks on appropriate antimicrobial therapy or if bacteremia recurs after a 6-week course of treatment. Tricuspid repair/reconstruction or valvectomy with valve replacement plus combined antipseudomonal regimen may be the optimal therapy for refractory right-sided endocarditis. This approach not only may prevent the development of severe and permanent impairment of right ventricular function, which is a complication of valvectomy alone without valve replacement, but also may cure the infection. For left-sided disease, surgery is recommended if blood cultures remain positive for 7 days on appropriate antimicrobial therapy or if *Pseudomonas* bacteremia recurs after completion of a 6-week course of the combined regimen.

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Internal Medicine

Caverzagie, K. J., E. C. Bernabeo, S. G. Reddy and E. S. Holmboe (2009). "The role of physician engagement on the impact of the hospital-based practice improvement module (PIM)." *J Hosp Med* 4(8): 466-70. [PDF Full-Text](#)

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BACKGROUND: Physicians play an important role in hospital quality improvement (QI) activities. The Hospital-Based Practice Improvement Module (Hospital PIM) is a web-based assessment tool designed by the American Board of Internal Medicine (ABIM) to facilitate physician involvement in QI as a part of maintaining certification. **OBJECTIVE:** The primary objective of this study is to explore the impact of the Hospital PIM on physicians participating in hospital-based QI. **DESIGN:** Qualitative design consisting of semistructured telephone interviews. **PARTICIPANTS:** A purposeful sample of 21 early-completers of the Hospital PIM. **MEASUREMENTS:** Grounded-theory analysis was used to analyze transcripts of the semistructured telephone interviews. **RESULTS:** Physician completers of the Hospital PIM describe the impact in a variety of ways, including new learning about QI principles and activities, added value to their practice, and enhanced QI

experience. An emerging theme was the mediating role of physician engagement in relation to the overall impact of the Hospital PIM. Four case studies illustrate these findings. Facilitators and barriers that influence the overall experience of the PIM are described. CONCLUSIONS: The impact of completing the Hospital PIM is mediated by the degree of physician engagement with the QI process. Physicians who become engaged with the Hospital PIM and QI process may be more likely to report successful experiences in implementing QI activities in hospital settings than those who do not become engaged.

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Nephrology

Besarab, A., W. H. Horl and D. Silverberg (2009). "Iron Metabolism, Iron Deficiency, Thrombocytosis, and the Cardiorenal Anemia Syndrome." *Oncologist* **14**: 22-33. [Article Request Form](#)

[Besarab, Anatole] Henry Ford Hosp, Div Nephrol & Hypertens, Dept Internal Med, Detroit, MI 48301 USA. [Besarab, Anatole] Wayne State Univ, Detroit, MI USA. [Hoerl, Walter Hermann] Med Univ Vienna, Dept Med 3, Div Nephrol & Dialysis, Vienna, Austria. [Silverberg, Donald] Tel Aviv Med Ctr & Sch Med, Dept Nephrol, Tel Aviv, Israel.

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In treating moderate to severe anemia of chronic kidney disease (CKD), oral iron is effective only in a minority of nondialysis patients. Intravenous iron is more effective and can raise levels of hemoglobin even without the use of erythropoiesis-stimulating agents (ESAs). Unfortunately, the current assays of iron status that are presently widely available are not especially helpful in predicting response. In patients on dialysis, i.v. iron is effective over a wide range of serum ferritin from <100 ng/ml to 800 ng/ml. None of the three available randomized controlled trials comparing oral with i.v. iron showed evidence of nephrotoxicity caused by i.v. iron. Iron deficiency is a risk factor for thrombocytosis and should, wherever possible, be avoided. Optimal coadministration of iron may reduce the risk for ESA-driven cardiovascular events. Increased total body iron stores (imperfectly reflected by serum ferritin levels in CKD) do not appear to be related to such events or hospitalization in CKD; it is unclear what other risk factors and mechanisms need to be considered. In the appreciable proportion of patients with both renal and cardiac dysfunction, management is further complicated by a vicious circle (which can be characterized as cardiorenal anemia syndrome) in which CKD, heart failure, and anemia exacerbate each other. In such patients, correction of anemia appears to improve cardiac function and quality of life without a greater risk for adverse events. *The Oncologist* 2009; 14(suppl 1): 22-33

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Neurology

Ascherio, A., P. A. Lewitt, K. Xu, S. Eberly, A. Watts, W. R. Matson, C. Marras, K. Kieburtz, A. Rudolph, M. B. Bogdanov, S. R. Schwid, M. Tennis, C. M. Tanner, M. F. Beal, A. E. Lang, D. Oakes, S. Fahn, I. Shoulson, M. A. Schwarzschild and D. I. for the Parkinson Study Group (2009). "Urate as a Predictor of the Rate of Clinical Decline in Parkinson Disease." *Arch Neurol* **EPub Ahead of Print**. [PDF Full-Text](#)

Harvard School of Public Health (Dr Ascherio), Channing Laboratory, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School (Dr Ascherio), and Department of Neurology, MassGeneral Institute for Neurodegenerative Disease, Massachusetts General Hospital (Drs Xu and Schwarzschild and Ms Tennis), Boston, and Bedford Veterans Administration Medical Center, Bedford (Drs Matson and Bogdanov); Department of Neurology, Henry Ford Hospital and Wayne State University School of Medicine, Detroit, Michigan (Dr LeWitt); Departments of Biostatistics (Ms Eberly, Mr Watts, and Dr Oakes) and Neurology (Drs Kieburtz, Rudolph, Schwid, and Shoulson), University of Rochester, Rochester, and Department of Neurology and Neuroscience, Cornell University (Dr Beal) and Department of Neurology, Columbia University (Dr Fahn), New York, New York; The Morton and Gloria Shulman Movement Disorders Centre, Toronto Western Hospital, University of Toronto, Toronto, Ontario, Canada (Drs Marras and Lang); and Department of Clinical Research, Parkinson's Institute, Sunnyvale, California (Dr Tanner).

BACKGROUND: The risk of Parkinson disease (PD) and its rate of progression may decline with increasing concentration of blood urate, a major antioxidant. **OBJECTIVE:** To determine whether serum and cerebrospinal fluid concentrations of urate predict clinical progression in patients with PD. **Design, Setting, and PARTICIPANTS:** Eight hundred subjects with early PD enrolled in the Deprenyl and Tocopherol Antioxidative

Therapy of Parkinsonism (DATATOP) trial. The pretreatment urate concentration was measured in serum for 774 subjects and in cerebrospinal fluid for 713 subjects. MAIN OUTCOME MEASURES: Treatment-, age-, and sex-adjusted hazard ratios (HRs) for clinical disability requiring levodopa therapy, the prespecified primary end point of the original DATATOP trial. RESULTS: The HR of progressing to the primary end point decreased with increasing serum urate concentrations (HR for highest vs lowest quintile = 0.64; 95% confidence interval [CI], 0.44-0.94; HR for a 1-SD increase = 0.82; 95% CI, 0.73-0.93). In analyses stratified by alpha-tocopherol treatment (2000 IU/d), a decrease in the HR for the primary end point was seen only among subjects not treated with alpha-tocopherol (HR for a 1-SD increase = 0.75; 95% CI, 0.62-0.89; vs HR for those treated = 0.90; 95% CI, 0.75-1.08). Results were similar for the rate of change in the Unified Parkinson's Disease Rating Scale score. Cerebrospinal fluid urate concentration was also inversely related to both the primary end point (HR for highest vs lowest quintile = 0.65; 95% CI, 0.44-0.96; HR for a 1-SD increase = 0.89; 95% CI, 0.79-1.02) and the rate of change in the Unified Parkinson's Disease Rating Scale score. As with serum urate concentration, these associations were present only among subjects not treated with alpha-tocopherol. CONCLUSIONS: Higher serum and cerebrospinal fluid urate concentrations at baseline were associated with slower rates of clinical decline. The findings strengthen the link between urate concentration and PD and the rationale for considering central nervous system urate concentration elevation as a potential strategy to slow PD progression. Published online October 12, 2009 (doi:10.1001/archneurol.2009.247).

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Neurology

Friedman, H. S., M. D. Prados, P. Y. Wen, T. Mikkelsen, D. Schiff, L. E. Abrey, W. K. A. Yung, N. Paleologos, M. K. Nicholas, R. Jensen, J. Vredenburgh, J. Huang, M. X. Zheng and T. Cloughesy (2009). "Bevacizumab Alone and in Combination With Irinotecan in Recurrent Glioblastoma." Journal of Clinical Oncology **27**(28): 4733-4740. [PDF Full-Text](#)

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Purpose We evaluated the efficacy of bevacizumab, alone and in combination with irinotecan, in patients with recurrent glioblastoma in a phase II, multicenter, open-label, noncomparative trial. Patients and Methods One hundred sixty-seven patients were randomly assigned to receive bevacizumab 10 mg/kg alone or in combination with irinotecan 340 mg/m² or 125 mg/m² (with or without concomitant enzyme-inducing antiepileptic drugs, respectively) once every 2 weeks. Primary end points were 6-month progression-free survival and objective response rate, as determined by independent radiology review. Secondary end points included safety and overall survival. Results In the bevacizumab-alone and the bevacizumab-plus-irinotecan groups, estimated 6-month progression-free survival rates were 42.6% and 50.3%, respectively; objective response rates were 28.2% and 37.8%, respectively; and median overall survival times were 9.2 months and 8.7 months, respectively. There was a trend for patients who were taking corticosteroids at baseline to take stable or decreasing doses over time. Of the patients treated with bevacizumab alone or bevacizumab plus irinotecan, 46.4% and 65.8%, respectively, experienced grade \geq 3 adverse events, the most common of which were hypertension (8.3%) and convulsion (6.0%) in the bevacizumab-alone group and convulsion (13.9%), neutropenia (8.9%), and fatigue (8.9%) in the bevacizumab-plus-irinotecan group. Intracranial hemorrhage was noted in two patients (2.4%) in the bevacizumab-alone group (grade 1) and in three patients (3.8%) patients in the bevacizumab-plus-irinotecan group (grades 1, 2, and 4, respectively). Conclusion Bevacizumab, alone or in combination with irinotecan, was well tolerated and active in recurrent glioblastoma.

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Neurology

Korzyukov, O., E. Asano, V. Gumenyuk, C. Juhasz, M. Wagner, R. D. Rothermel and H. T. Chugani (2009). "Intracranial Recording and Source Localization of Auditory Brain

Responses Elicited at the 50 ms Latency in Three Children Aged from 3 to 16 Years." Brain Topography **22**(3): 166-175. [PDF Full-Text](#)

[Korzyukov, Oleg] MRC, Cognit & Brain Sci Unit, Cambridge CB2 7EF, England. [Korzyukov, Oleg; Asano, Eishi; Juhasz, Csaba; Chugani, Harry T.] Wayne State Univ, Carman & Ann Adams Dept Pediat, Childrens Hosp Michigan, Detroit, MI 48201 USA. [Asano, Eishi; Juhasz, Csaba; Chugani, Harry T.] Wayne State Univ, Childrens Hosp Michigan, Dept Neurol, Detroit, MI 48201 USA. [Gumenyuk, Valentina] Henry Ford Hosp, Dept Neurol, Detroit, MI 48202 USA. [Chugani, Harry T.] Wayne State Univ, Childrens Hosp Michigan, Dept Radiol, Detroit, MI 48201 USA. [Wagner, Michael] Compumed Neuroscan, D-20255 Hamburg, Germany. [Rothermel, Robert D.] Childrens Hosp Michigan, Dept Psychiat & Psychol, Detroit, MI 48201 USA. Korzyukov, O, MRC, Cognit & Brain Sci Unit, 15 Chaucer Rd, Cambridge CB2 7EF, England. okorzyuk@med.wayne.edu

Maturational studies of the auditory-evoked brain response at the 50 ms latency provide an insight into why this response is aberrant in a number of psychiatric disorders that have developmental origin. Here, using intracranial recordings we found that neuronal activity of the primary contributors to this response can be localised at the lateral part of Heschl's gyrus already at the age of 3.5 years. This study provides results to support the notion that deviations in cognitive function(s) attributed to the auditory P50 in adults might involve abnormalities in neuronal activity of the frontal lobe or in the interaction between the frontal and temporal lobes. Validation and localisation of progenitors of the adults' P50 in young children is a much-needed step in the understanding of the biological significance of different subcomponents that comprise the auditory P50 in the adult brain. In combination with other approaches investigating neuronal mechanisms of auditory P50, the present results contribute to the greater understanding of what and why neuronal activity underlying this response is aberrant in a number of brain dysfunctions. Moreover, the present source localisation results of auditory response at the 50 ms latency might be useful in paediatric neurosurgery practice.

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Neurology

LeWitt, P. A., D. Jennings, K. E. Lyons, R. Pahwa, A. L. Rabinowicz, J. Wang, M. Guarnieri, J. P. Hubble and H. Murck (2009). "Pharmacokinetic-pharmacodynamic crossover comparison of two levodopa extension strategies." Mov Disord **24**(9): 1319-24. [PDF Full-Text](#)

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Controlled-release carbidopa and levodopa (CL-CR) and the combination of carbidopa, levodopa, and entacapone (CLE) are used for extending levodopa (L-dopa) effects. In a randomized, open-label crossover study of 17 PD subjects with wearing-off responses, we compared 8-hour L-dopa pharmacokinetics (PK) and clinical effects after two doses of CL-CR (50 and 200 mg, respectively) and CLE (37.7, 150, 200 mg, respectively). PK analysis revealed the anticipated near-equivalent mean L-dopa area-under-the-concentration-curve values (639,490 ng min/mL for two doses of CLE, and 662,577 for CL-CR, $P = 0.86$). The mean hourly fluctuation index for L-dopa concentration was 235% for CLE and 196% for CL-CR ($P = 0.004$). The mean maximal concentration for the first CLE dose was 1,926 +/- 760 ng/mL and for CL-CR, 1,840 +/- 889 ($P = 0.33$). During the PK studies, the mean time that L-dopa concentration was $\geq 1,000$ ng/mL for CLE was 291 +/- 88 minutes and for CL-CR, 306 +/- 86 ($P = 0.33$). The mean percent-time in "off" state was 18% for CLE and 28% for CL-CR ($P = 0.017$), "on state without dyskinesia" was 64% for CLE and 65% for CL-CR ($P = 0.803$), and "on state with nontroublesome dyskinesia" was 18% for CLE and 7% for CL-CR ($P = 0.03$). Despite less "off" time with CLE, both formulations demonstrated similar mean PK values and marked intersubject PK variability.

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Neurology

Liu, X. S., M. Chopp, R. L. Zhang, A. Hozeska-Solgot, S. C. Gregg, B. Buller, M. Lu and Z. G. Zhang (2009). "Angiopoietin 2 mediates the differentiation and migration of neural progenitor cells in the subventricular zone after stroke." J Biol Chem **284**(34): 22680-9. PMC2755676. [PDF Full-Text](#)

Department of Neurology, Henry Ford Health System, Detroit, Michigan 48202, USA.

Ischemic stroke stimulates neurogenesis in the adult rodent brain. The molecules underlying stroke-induced neurogenesis have not been fully investigated. Using real-time reverse transcription-PCR, we found that stroke substantially up-regulated angiopoietin 2 (ANG2), a proangiogenic gene, expression in subventricular zone neural progenitor cells. Incubation of neural progenitor cells with recombinant human ANG2 significantly increased the number of beta-III tubulin-positive cells, a marker of immature neurons, but did not alter the number of glial fibrillary acidic protein (GFAP)-positive cells, a marker of astrocytes, suggesting that ANG2 promotes neuronal differentiation. Blockage of the ANG2 receptor, Tie2, with small interference RNA (siRNA)-Tie2 attenuated recombinant human ANG2 (rhANG2)-increased beta-III tubulin mRNA levels compared with levels in the progenitor cells transfected with control siRNA. Chromatin immunoprecipitation analysis revealed that CCAAT/enhancer-binding protein (C/EBP beta) up-regulated by rhANG2 bound to beta-III tubulin, which is consistent with published data that there are several C/EBP beta binding sites in the promoter of beta-III tubulin gene. In addition, rhANG2 enhanced migration of neural progenitor cells measured by single neurosphere assay. Blockage of Tie2 with siRNA-Tie2 and a Tie2-neutralizing antibody did not suppress ANG2-enhanced migration. However, inhibition of matrix metalloproteinases with GM6001 blocked ANG2-enhanced migration. Collectively, our data suggest that interaction of ANG2, a proangiogenic factor, with its receptor Tie2 promotes neural progenitor cell differentiation into neuronal lineage cells, whereas ANG2 regulates neural progenitor cell migration through matrix metalloproteinases, which do not require its receptor Tie2.

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Neurology

Oertel, W., P. LeWitt, F. Grieger, L. Bauer and B. Boroojerdi (2009). "Treatment of patients with early and advanced Parkinson's disease with transdermal rotigotine: age relationship to safety and tolerability." European Journal of Neurology **16**: 532-532. [Article Request Form](#)

[Oertel, W.] Univ Marburg, Marburg, Germany. [LeWitt, P.] Henry Ford Hosp, Southfield, MI USA. [Grieger, F.; Boroojerdi, B.] Schwarz Biosci, Monheim, Germany. [Bauer, L.] UCB Pharma SA NV, Brussels, Belgium.

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Neurology

Schuh, L. A., Z. London, R. Neel, C. Brock, B. M. Kissela, L. Schultz and D. J. Gelb (2009). "Education research: Bias and poor interrater reliability in evaluating the neurology clinical skills examination." Neurology **73**(11): 904-8. [PDF Full-Text](#)

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OBJECTIVE: The American Board of Psychiatry and Neurology (ABPN) has recently replaced the traditional, centralized oral examination with the locally administered Neurology Clinical Skills Examination (NEX). The ABPN postulated the experience with the NEX would be similar to the Mini-Clinical Evaluation Exercise, a reliable and valid assessment tool. The reliability and validity of the NEX has not been established. **METHODS:** NEX encounters were videotaped at 4 neurology programs. Local faculty and ABPN examiners graded the encounters using 2 different evaluation forms: an ABPN form and one with a contracted rating scale. Some NEX encounters were purposely failed by residents. Cohen's kappa and intraclass correlation coefficients (ICC) were calculated for local vs ABPN examiners. **RESULTS:** Ninety-eight videotaped NEX encounters of 32 residents were evaluated by 20 local faculty evaluators and 18 ABPN examiners. The interrater reliability for a determination of pass vs fail for each encounter was poor (kappa 0.32; 95% confidence interval [CI] = 0.11, 0.53). ICC between local faculty and ABPN examiners for each performance rating on the ABPN NEX form was poor to moderate (ICC range 0.14-0.44), and did not improve with the contracted rating form (ICC range 0.09-0.36). ABPN examiners were more likely than local examiners to fail residents. **CONCLUSIONS:** There is poor interrater reliability between local faculty and American Board of Psychiatry and Neurology examiners. A bias was detected for favorable assessment locally, which is concerning for the validity of the examination. Further study is needed to assess whether training can improve interrater reliability and offset bias.

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Neurology

Szalad, A., M. Katakowski, X. G. Zheng, F. Jiang and M. Chopp (2009). "Transcription factor Sp1 induces ADAM17 and contributes to tumor cell invasiveness under hypoxia." Journal of Experimental & Clinical Cancer Research **28**. [Article Request Form](#)

[Katakowski, Mark; Zheng, Xuguang; Jiang, Feng; Chopp, Michael] Henry Ford Hosp, Dept Neurol, Detroit, MI 48202 USA. [Szalad, Alexandra; Chopp, Michael] Oakland Univ, Dept Phys, Rochester, MI 48309 USA. Chopp, M, Henry Ford Hosp, Dept Neurol, Detroit, MI 48202 USA. ajciungu@yahoo.com
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Background: Expression of the Sp1 transcription factor is induced by hypoxia, and the ADAM17 promoter contains predicted Sp1 binding sites. ADAM17 contributes to hypoxic-induced invasiveness of glioma. In this study, we investigated whether Sp1 transcription factor induces ADAM17 and/or contributes to tumor cell invasiveness in hypoxia. Methods: Employing RT-PCR and Western blot, we examined the role of Sp1 in ADAM17 transcription/expression under normoxic and hypoxic conditions, and whether it binds to the ADAM17 GC-rich promoter region using a chromatin immunoprecipitation assay. Additionally, we tested the effect of Sp1 suppression in tumor cell invasion and migration, using Matrigel basement membrane invasion chambers, a scratch wound-healing assay, and small interfering RNA. Results: Here, we found that Sp1 binds to the ADAM17 promoter, and that Sp1 regulates ADAM17 expression under hypoxia. Furthermore, suppression of Sp1 decreases invasiveness and migration in U87 tumor cells. Conclusion: Our findings suggest the Sp1 transcription factor mediates ADAM17 expression under hypoxia, regulates glioma invasiveness, and thus, may be a target for anti-invasion therapies.

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Neurology

Varelas, P. N., L. Haccin-Bey, L. Schultz, M. Conti, M. V. Spanaki and T. A. Gennarelli (2009). "Withdrawal of life support in critically ill neurosurgical patients and in-hospital death after discharge from the neurosurgical intensive care unit. Clinical article." J Neurosurg **111**(2): 396-404. [PDF Full-Text](#)

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OBJECT: The aim of this study was to examine the variables influencing the mode and location of death in patients admitted to a neurosurgical intensive care unit (NICU), including the participation of a newly appointed neurointensivist (NI). METHODS: Data from all patients admitted to a university hospital NICU were prospectively collected and compared between 2 consecutive 19-month periods before and after the appointment of an NI. RESULTS: One thousand eighty-seven patients were admitted before and 1279 after the NI's appointment. The withdrawal of life support (WOLS) occurred in 52% of all cases of death. Death following WOLS compared with survival was independently associated with an older patient age (OR 1.04/year, 95% CI 1.03-1.05), a higher University Hospitals Consortium (UHC) expected mortality rate (OR 1.05/%, 95% CI 1.04-1.07), transfer from another hospital (OR 3.7, 95% CI 1.6-8.4) or admission through the emergency department (OR 5.3, 95% CI 2.4-12), admission to the neurosurgery service (OR 7.5, 95% CI 3.2-17.6), and diagnosis of an ischemic stroke (OR 5.4, 95% CI 1.4-20.8) or intracerebral hemorrhage (OR 5.7, 95% CI 1.9-16.7). On discharge from the NICU, 54 patients died on the hospital ward (2.7% mortality rate). A younger patient age (OR 0.94/year, 95% CI 0.92-0.96), higher UHC-expected mortality rate (OR 1.01/%, 95% CI 1-1.03), and admission to the neurosurgery service (OR 9.35, 95% CI 1.83-47.7) were associated with death in the NICU rather than the ward. There was no association between the participation of an NI and WOLS or ward mortality rate. CONCLUSIONS: The mode and location of death in NICU-admitted patients did not change after the appointment of an NI. Factors other than the participation of an NI-including patient age and the severity and type of neurological injury-play a significant role in the decision to withdraw life support in the NICU or dying in-hospital after discharge from the NICU.

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Neurology

Varelas, P. N. and M. A. Mirski (2009). "Status epilepticus." Curr Neurol Neurosci Rep **9**(6): 469-76. [PDF Full-Text](#)

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Status epilepticus (SE) still results in significant mortality and morbidity. Whereas mortality depends mainly on the age of the patient as well as etiology, morbidity often results from a myriad of complications that occur during prolonged admission to an intensive care environment. Although SE is a clinical diagnosis in most cases (convulsant), its treatment requires support by continuous electroencephalographic recording to ensure cessation of potential nonconvulsive elements of SE. Treatment must be initiated as early as possible and consists of benzodiazepine administration and supportive measures for the airway and circulation. These initial interventions are followed by effective intravenous antiepileptic drugs. If the SE becomes refractory, more complex intensive care interventions, such as induction of barbiturate coma, need to be pursued. Data regarding the role of more recently available antiepileptic drugs in treating SE also are discussed in this review.

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Neurology

Zhang, J., Z. G. Zhang, D. Morris, Y. Li, C. Roberts, S. B. Elias and M. Chopp (2009). "Neurological functional recovery after thymosin beta4 treatment in mice with experimental auto encephalomyelitis." Neuroscience **EPub Ahead of Print**. [PDF Full-Text](#)

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In the present study, we hypothesized that thymosin beta 4 (Tbeta4) is a potential therapy of multiple sclerosis (MS). To test this hypothesis, SJL/J mice (n=21) were subjected to experimental autoimmune encephalomyelitis (EAE), an animal model of MS. EAE mice were treated with saline or Tbeta4 (6 mg/kg, n=10) every 3 days starting on the day of myelin proteolipid protein (PLP) immunization for total five doses. Neurological function, inflammatory infiltration, oligodendrocyte progenitor cells (OPCs) and mature oligodendrocytes were measured in the brain of EAE mice. Double immunohistochemical staining was used to detect proliferation and differentiation of OPCs. Tbeta4 was used to treat N20.1 cells (premature oligodendrocyte cell line) in vitro, and proliferation of N20.1 cells was measured by bromodeoxyuridine (BrdU) immunostaining. Tbeta4 treatment improved functional recovery after EAE. Inflammatory infiltrates were significantly reduced in the Tbeta4 treatment group compared to the saline groups (3.6±0.3/slide vs 5±0.5/slide, P<0.05). NG2(+) OPCs (447.7±41.9 vs 195.2±31/mm²) in subventricular zone (SVZ), 75.1±4.7 vs 41.7±3.2/mm² in white matter), CNPase(+) mature oligodendrocytes (267.5±10.3 vs 141.4±22.9/mm²), BrdU(+) with NG2(+) OPCs (32.9±3.7 vs 17.9±3.6/mm²), BrdU(+) with CNPase(+) mature oligodendrocytes (18.2±1.7 vs 10.7±2.2/mm²) were significantly increased in the Tbeta4 treated mice compared to those of saline controls (P<0.05). These data indicate that Tbeta4 treatment improved functional recovery after EAE, possibly, via reducing inflammatory infiltrates, and stimulating oligodendrogenesis.

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Neurology

Zhang, Y. L., Y. Xiong, A. Mahmood, Y. L. Meng, C. S. Qu, T. Schallert and M. Chopp (2009). "Therapeutic effects of erythropoietin on histological and functional outcomes following traumatic brain injury in rats are independent of hematocrit." Brain Research **1294**: 153-164. [PDF Full-Text](#)

[Zhang, Yanlu; Xiong, Ye; Mahmood, Asim; Meng, Yuling; Qu, Changsheng] Henry Ford Hlth Syst, Dept Neurosurg, Detroit, MI 48202 USA. [Chopp, Michael] Henry Ford Hlth Syst, Dept Neurol, Detroit, MI 48202 USA. [Chopp, Michael] Oakland Univ, Dept Phys, Rochester, MI 48309 USA. [Schallert, Timothy] Univ Texas Austin, Dept Psychol, Austin, TX 78712 USA. [Schallert, Timothy] Univ Texas Austin, Inst Neurosci, Austin, TX 78712 USA.

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Erythropoietin (EPO) provides neuroprotection and neurorestoration after traumatic brain injury (TBI). The EPO doses used for treatment of TBI significantly increase hematocrit, which may affect the efficacy of EPO therapy for TBI. The aim of this study was to investigate whether normalization of hematocrit would affect EPO efficacy for treatment of TBI. Young adult male Wistar rats were randomly divided into four groups: (1) Sham group (n = 6); (2) TBI+saline group (n = 6); (3) TBI+EPO group (n = 6); and (4) TBI+EPO+hemodilution group (n = 7). TBI was induced by controlled cortical impact over the left parietal cortex. EPO (5,000 U/kg) or saline was

administered intraperitoneally at days 1, 2, and 3 postinjury. Neurological function was assessed using a modified neurological severity score (mNSS), footfault and the Morris water maze (MWM) tests. Animals were sacrificed 35 days after injury, and brain sections were stained for immunohistochemistry. Compared to the saline treatment, EPO treatment significantly reduced hippocampal cell loss, enhanced angiogenesis and neurogenesis in the injured cortex and hippocampus, and significantly improved sensorimotor functional outcome (lowered mNSS and foot faults) and spatial learning (MWM test). Normovolemic hemodilution effectively normalized the hematocrit and did not significantly affect the histological and functional outcome of EPO therapy for TBI. These data for the first time demonstrate that increased hematocrit does not affect therapeutic effects of EPO on histological and long-term functional outcomes in rats after TBI and also suggest that neuroprotection and neurorestoration of EPO treatment are independent of hematocrit. (C) 2009 Elsevier B.V. All rights reserved.

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Neurosurgery

Hong, X., K. K. Nelson, A. C. Decarvalho and S. N. Kalkanis (2009). "Heparanase expression of glioma in human and animal models." J Neurosurg **EPub Ahead of Print**. [PDF Full-Text](#)

Department of Neurosurgery, Henry Ford Health System, Detroit, Michigan.

Object Mammalian heparanase has been shown to function in tumor progression, invasion, and angiogenesis. However, heparanase expression in gliomas has not been well analyzed. To clarify its expression in gliomas, human glioma tissues and glioma animal models were investigated. Methods The expression of heparanase mRNA was determined in 33 resected human glioma tissues by semiquantitative real-time polymerase chain reaction. Heparanase expression was verified with a Western blot assay and immunohistochemistry (IHC) staining. Primary neurospheres from human glioblastoma multiforme (GBM) were developed in vitro. Heparanase expression in murine astrocytoma and human primary neurosphere animal models was examined using IHC. Results The authors found that heparanase mRNA is greatly increased in gliomas including oligodendroglioma (9 samples), anaplastic astrocytoma (11 samples), and GBM (13 samples) as compared with healthy brain mRNA (3 samples). Note, however, that no significant difference was observed among the 3 tumor groups. Increased heparanase expression was also found in tumor tissues on Western blotting. Immunohistochemistry staining demonstrated that heparanase was expressed by neovessel endothelial cells, infiltrated neutrophils, and in some cases, by neoplastic cells. Heparanase-expressing cells, including GBM tumor cells and neovessel endothelial cells, exhibited decreased expression of CD44, a cell adhesion molecule on the cell membrane that is important for regulating tumor invasion. In addition, heparanase-expressing tumor cells showed an elevated density of the cell proliferation marker Ki 67, as compared with its density in non-heparanase-expressing tumor cells, suggesting that heparanase expression is correlated with enhanced tumor proliferation. Two animal glioma models were tested for heparanase expression. Both murine astrocytoma cells (Ast11.9-2) and cultured primary human GBM neurospheres expressed heparanase when grown in animal brain tissue. Conclusions Glioma tissues contain increased levels of heparanase. Multiple cell types contribute to the expression of heparanase, including neovessel endothelial cells, tumor cells, and infiltrated neutrophils. Heparanase plays an important role in the control of cell proliferation and invasion. Animal models using Ast11.9-2 and primary neurospheres are suitable for antitumor studies targeting heparanase.

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Neurosurgery

Karki, K., R. A. Knight, Y. X. Han, D. M. Yang, J. F. Zhang, K. A. Ledbetter, M. Chopp and D. M. Seyfried (2009). "Simvastatin and Atorvastatin Improve Neurological Outcome After Experimental Intracerebral Hemorrhage." Stroke **40**(10): 3384-3389. [PDF Full-Text](#)

[Han, Yuxia; Yang, Dongmei; Zhang, Jianfeng; Seyfried, Donald M.] Henry Ford Hosp, Dept Neurosurg, Detroit, MI 48202 USA. [Karki, Kishor; Knight, Robert A.; Ledbetter, Karyn A.; Chopp, Michael] Henry Ford Hosp, Dept Neurol, Detroit, MI 48202 USA. [Karki, Kishor; Knight, Robert A.; Chopp, Michael] Oakland Univ, Dept Phys, Rochester, MI USA.

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Background and Purpose-This study investigates the effects of statin treatment on experimental intracerebral hemorrhage (ICH) using behavioral, histological, and MRI measures of recovery. Methods-Primary ICH was

induced in rats. Simvastatin (2 mg/kg), atorvastatin (2 mg/kg), or phosphate-buffered saline (n = 6 per group) was given daily for 1 week. MRI studies were performed 2 to 3 days before ICH, and at 1 to 2 hours and 1, 2, 7, 14, and 28 days after ICH. The ICH evolution was assessed via hematoma volume measurements using susceptibility-weighted imaging (SWI) and tissue loss using T-2 maps and hematoxylin and eosin (H&E) histology. Neurobehavioral tests were done before ICH and at various time points post-ICH. Additional histological measures were performed with doublecortin neuronal nuclei and bromodeoxyuridine stainings. Results-Initial ICH volumes determined by SWI were similar across all groups. Simvastatin significantly reduced hematoma volume at 4 weeks (P = 0.002 versus control with acute volumes as baseline), whereas that for atorvastatin was marginal (P = 0.09). MRI estimates of tissue loss (% of contralateral hemisphere) for treated rats were significantly lower (P = 0.0003 and 0.001, respectively) than for control at 4 weeks. Similar results were obtained for H&E histology (P = 0.0003 and 0.02, respectively). Tissue loss estimates between MRI and histology were well correlated (R-2 = 0.764, P < 0.0001). Significant improvement in neurological function was seen 2 to 4 weeks post-ICH with increased neurogenesis observed. Conclusions-Simvastatin and atorvastatin significantly improved neurological recovery, decreased tissue loss, and increased neurogenesis when administered for 1 week after ICH. (Stroke. 2009;40:3384-3389.)

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Neurosurgery

Krishnamurthy, S., A. Navarro-Martin and A. Maitz (2009). "Gamma Knife radiosurgery for occipital condyle metastasis." Clinical & Translational Oncology **11**(9): 622-624. [PDF Full-Text](#)

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We present a 45 year old female with right occipital condylar metastases who was treated at William Beaumont Hospital in the Gamma Knife Unit. Clinical results at 17 months follow-up and MRI are exposed.

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Neurosurgery

McIntosh, K., N. Roosen and H. Huraibi (2009). "Spinal cord stimulation (SCS) implant experiences in treating intractable chronic pain syndromes in a neurosurgery and pain management private practice." European Journal of Neurology **16**: 90-90. [Article Request Form](#)

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Neurosurgery

Qu, C. S., Y. Xiong, A. Mahmood, D. L. Kaplan, A. Goussev, R. Z. Ning and M. Chopp (2009). "Treatment of traumatic brain injury in mice with bone marrow stromal cell-impregnated collagen scaffolds Laboratory investigation." Journal of Neurosurgery **111**(4): 658-665. [PDF Full-Text](#)

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Object. This study was designed to investigate new ways of delivering human marrow stromal cells (hMSCs) to the injured brain by impregnating them into collagen scaffolds in a mouse model of traumatic brain injury (TBI). Methods. Eight C57BL/6 J mice were injured with controlled cortical impact and received transplantation into the lesion cavity of 0.3×10^6 hMSCs impregnated into 3D porous collagen scaffolds. Additional experimental groups of 8 mice each received scaffolds implanted alone into the lesion cavity, hMSCs administered alone intracerebrally or intravenously, or saline injected into the lesion core. All treatments were performed 7 days after TBI. Spatial learning was measured using a modified Morris water maze test, and brain tissue samples were processed for histopathological analysis. Results. The results showed that hMSC-impregnated scaffolds were more effective than hMSCs administered alone (either intravenously or intracerebrally) in improving spatial learning, reducing lesion volume, and increasing vascular density after TBI. Conclusions. Collagen scaffolds populated with hMSCs may be a new way to reconstruct injured brain tissue and improve neurological function after TBI. (DOI: 10.3171/2009.4.JNS081681)

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Neurosurgery

Torcuator, R., R. Zuniga, Y. S. Mohan, J. Rock, T. Doyle, J. Anderson, J. Gutierrez, S. Ryu, R. Jain, M. Rosenblum and T. Mikkelsen (2009). "Initial experience with bevacizumab treatment for biopsy confirmed cerebral radiation necrosis." *J Neurooncol* **94**(1): 63-8. [PDF Full-Text](#)

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BACKGROUND: Cerebral radiation necrosis is a serious complication of radiation treatment for brain tumors. Therapeutic options include corticosteroids, anticoagulation and hyperbaric oxygen with limited efficacy. Bevacizumab, an antibody against VEGF had been reported to reduce edema in patients with suspected radiation necrosis. We retrospectively reviewed 6 patients with biopsy proven cerebral radiation necrosis treated with bevacizumab between 2006 and 2008. RESULTS: Interval MRI follow-up demonstrated radiographic response in all patients with an average reduction of 79% for the post gadolinium studies and 49% for the FLAIR images. The initial partial radiographic response was noted for up to a mean follow-up time of 5.9 months (6 weeks to 18 months). CONCLUSION: Bevacizumab appears to produce radiographic response and clinical benefits in the treatment of patients with cerebral radionecrosis.

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Neurosurgery

Torcuator, R. G., R. Thind, M. Patel, Y. S. Mohan, J. Anderson, T. Doyle, S. Ryu, R. Jain, L. Schultz, M. Rosenblum and T. Mikkelsen (2009). "The role of salvage reirradiation for malignant gliomas that progress on bevacizumab." *J Neurooncol* **Epub Ahead of Print**. [PDF Full-Text](#)

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Bevacizumab and irinotecan are effective against recurrent malignant gliomas. However, at subsequent progression, patients rarely respond to a second bevacizumab-containing chemotherapeutic regimen. Salvage re-irradiation with bevacizumab for recurrent but bevacizumab naive malignant gliomas showed encouraging results. We performed a retrospective review of the medical records of 23 patients treated with either fractionated stereotactic radiotherapy (FSRT) or stereotactic radiosurgery (SRS) after progression on an initial bevacizumab regimen. Patients were treated after re-irradiation with bevacizumab but combined with a different chemotherapy. We then compared them to another 23 patients who progressed on an initial bevacizumab + chemotherapy regimen. These patients did not receive re-irradiation but bevacizumab was continued combined with a different chemotherapy. Patients treated with FSRT/SRS/bevacizumab had a longer median progression-free period (2.6 vs. 1.7 months, $P = 0.009$), longer median post FSRT/SRS treatment survival (7.2 vs. 3.3 months, $P = 0.03$) and higher radiographic response rate (22 vs. 0%, $P = 0.049$). FSRT or SRS followed by bevacizumab + chemotherapy may have a role for patients who progress on bevacizumab.

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Other

Brown, A. R., P. Coppola, M. Giacona, A. Petriches and M. A. Stockwell (2009). "Faith Community Nursing Demonstrates Good Stewardship of Community Benefit Dollars Through Cost Savings and Cost Avoidance." Family & Community Health **32**(4): 330-338. [PDF Full-Text](#)

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Health systems seeking responsible stewardship of community benefit dollars supporting Faith Community Nursing Networks require demonstration of positive measurable health outcomes. Faith Community Nurses (FCNs) answer the call for measurable outcomes by documenting cost savings and cost avoidances to families, communities, and health systems associated with their interventions. Using a spreadsheet tool based on Medicare reimbursements and diagnostic-related groupings, 3 networks of FCNs have together shown more than 600 000 (for calendar year 2008) healthcare dollars saved by avoidance of unnecessary acute care visits and extended care placements. The cost-benefit ratio of support dollars to cost savings and cost avoidance demonstrates that support of FCNs is good stewardship of community benefit dollars.

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Otolaryngology

Ghanem, T. A. and M. K. Wax (2009). "A novel split-thickness skin graft donor site: the radial skin paddle." Otolaryngol Head Neck Surg **141**(3): 390-4. [PDF Full-Text](#)

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OBJECTIVE: To eliminate morbidity of the thigh split-thickness skin graft (STSG) donor site in forearm flaps, the feasibility of harvesting from an alternate site was assessed. STUDY DESIGN: Case series with planned data collection. SETTING: A tertiary care academic setting. SUBJECTS AND METHODS: Data were collected from patients undergoing forearm flap reconstruction over 13 months. The forearm flap harvesting procedure was modified to incorporate STSG harvest directly from the flap skin paddle. RESULTS: There were 66 patients in this cohort, with mean age of 62.6 years. There were 58 fasciocutaneous radial forearm free flaps (RFFFs), three osteocutaneous RFFF, three ulnar flaps, and two reverse-flow RFFFs. The majority of flaps were used for mucosal coverage (n = 54), but 12 flaps were used for external skin coverage. The mean forearm defect was 36.5 cm² (12-77 cm²). Harvesting from the forearm skin paddle was successful in 64 patients (97%). Two patients required a thigh STSG; both patients were octogenarians with frail skin. CONCLUSION: A thigh STSG donor site, with its associated morbidities, can be eliminated in 97 percent of patients undergoing forearm flaps. Older patients with frail skin may require a thigh donor site.

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Otolaryngology

Worsham, M. J., U. Raju, M. Lu, A. Kapke, A. Botttrel, J. F. Cheng, V. Shah, A. Savera and S. R. Wolman (2009). "Risk factors for breast cancer from benign breast disease in a diverse population." Breast Cancer Research and Treatment **118**(1): 1-7. [PDF Full-Text](#)

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Background The majority of studies have reported risks of breast cancer (BC) from benign breast disease (BBD) in essentially homogenous Caucasian populations. Information on breast cancer risk factors in larger, multi-ethnic populations should facilitate the development of appropriate and targeted risk reduction strategies. Design Cases and controls were drawn from a parent BBD cohort of 4,970 women, 1,341 African-Americans (AA) and 3,629 non-AA who were diagnosed with BBD after examination of an excisional breast biopsy. Risk factors (34 variables) included demographics, lesion types, and epidemiological variables. Results The final multivariable model retained significance ($P < 0.05$) for lesion risk-level, fibroadenoma, and the interaction of age-by-race. Women with proliferative lesions (no atypia, risk level 2) were 1.7 times more likely to develop BC when compared with women with non-proliferative lesions (OR = 1.7, 95% CI 1.13, 2.42, $P = 0.009$). Women with atypia (risk level 3) were 3.75 times more likely to develop BC compared to women with non-proliferative lesions (OR = 3.75, 95% CI 1.99, 7.06, $P < 0.001$). The odds of breast cancer was approximately 35% lower among women with fibroadenoma as compared to women without fibroadenoma (OR = 0.65, 95% CI 0.46, 0.94, $P = 0.020$). AA women with BBD who were 50 years or older were 2.28 times more likely to develop breast cancer as compared to non-AA women who were less than 50 years old (OR = 2.28, 95% CI 1.34, 3.88, $P = 0.002$). Conclusion Women with fibroadenoma (nonproliferative or proliferative) were less likely to progress to BC. Older AA women are at greater risk for progression to breast cancer from BBD.

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Pathology

Cankovic, M., L. Whiteley, R. C. Hawley, R. J. Zarbo and D. Chitale (2009). "Clinical performance of JAK2 V617F mutation detection assays in a molecular diagnostics laboratory: evaluation of screening and quantitation methods." *Am J Clin Pathol* **132**(5): 713-21. [PDF Full-Text](#)

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The presence of the JAK2 V617F mutation is now part of clinical diagnostic algorithms, and JAK2 status is routinely assessed when BCR/ABL- chronic myeloproliferative neoplasms (MPNs) are suspected. The aim of this study was to evaluate performance of 3 screening and 1 quantitative method for JAK2 V617F detection. For the study, 43 samples (27 bone marrow aspirates and 16 peripheral blood samples) were selected. The screening assays were the JAK2 Activating Mutation Assay (InVivoScribe, San Diego, CA), JAK2 MutaScreen kit (Ipsogen, Luminy Biotech, Marseille, France), and a home-brew melting curve analysis method. Ipsogen's JAK2 MutaQuant assay was used for quantification of mutant and wild-type alleles. The limit of detection was 1% for the kit-based screening methods and 10% for the melting curve method. The JAK2 MutaQuant assay demonstrated analytic sensitivity of 0.01%. All 4 methods detected cases of BCR/ABL- MPNs and gave negative results with BCR/ABL+ chronic myelogenous leukemia, multiple myeloma, myelodysplastic syndrome, and normal cases.

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Pathology

Kryvenko, O. N., O. M. Alassi, D. A. Chitale, N. S. Gupta, A. H. Ormsby and M. W. Lee (2009). "Angiolipoma of the Breast." *American Journal of Clinical Pathology* **132**(4): 31. [Article Request Form](#)

[Kryvenko, Oleksandr N.; Alassi, Osama M.; Chitale, Dhananjay A.; Gupta, Nilesh S.; Ormsby, Adrian H.; Lee, Min W.] Henry Ford Hosp, Detroit, MI 48202 USA.

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Pathology

Stark, A., D. Schultz, A. Kapke, P. Nadkarni, M. Burke, M. Linden and U. Raju (2009). "Obesity and risk of the less commonly diagnosed subtypes of breast cancer." *Ejso* **35**(9): 928-935.

[Article Request Form](#)

[Stark, A.; Schultz, D.; Linden, M.; Raju, U.] Henry Ford Hlth Syst, Dept Pathol, Detroit, MI 48202 USA. [Stark, A.; Nadkarni, P.] Geisinger Hlth Syst, Ctr Hlth Serv Res, Danville, PA USA. [Stark, A.] Univ Penn, Sch Med, Ctr Clin Epidemiol & Biostat, Philadelphia, PA 19104 USA. [Kapke, A.] Henry Ford Hlth Syst, Dept Biostat & Res Epidemiol, Detroit, MI 48202 USA. [Burke, M.] Henry Ford Hlth Syst, Dept Radiol, Detroit, MI 48202 USA.

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Objectives: A set of common epidemiologic risk factors have been associated with the risk of breast cancer despite of its molecular sub-classifications. We implemented a case series study with the primary objective of evaluating if obesity is associated with the diagnostic risk of "ER+ and/or PR+, HER2(+)", "ER-/PR-, HER2(-)", or "ER-/PR-, HER2(+)" relative to the most commonly diagnosed subtype of breast carcinoma, "ER+ and/or PR+, HER2(-)". **Methods:** Demographic, clinical and pathologic data were collected from existing databases. The statuses of HER2/neu biomarker and hormone receptors were dichotomized as either positive or negative. Immunohistochemical staining was used to assess the prevalence of different subtypes. Body mass index was calculated from weight and height data collected at the time of consultation. **Conclusions:** Findings from the present study suggest that excess body weight decreases the diagnostic risk of "ER-/PR-, HER2(-)", or "ER-/PR-, HER2(+)" relative to "ER+ and/or PR+, HER2(-)". Obese and overweight women are more likely to be diagnosed with "ER+ and/or PR+, HER2(-)", the subtype that has best prognosis and mostly associated with personal lifestyle. Weight gain with the population attributable-risk factor of 21.3% contributes the most to the incidence of invasive post menopausal breast cancer. Younger pre-menopausal women were more likely to be diagnosed with "ER+ and/or PR+, HER2(+)". In younger women biology of breast cancers with positive expression for hormone receptors and epidermal growth factor is a complex that extends beyond the currently assessed prognostic markers. (C) 2008 Elsevier Ltd. All rights reserved.

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Pediatrics

Conway, K., K. Shepard, S. S. Vandebush and A. Roffe (2009). "Improving access to oral health care through a school-based health center in Detroit, Michigan." [Am J Pub Health EPub Ahead of Print](#). [Article Request Form](#)

Henry Ford Health System, Pediatrics, School-Based and Community Health Program Oral Health Program, Detroit, Michigan.

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Pharmacy

Jennings, D. L. and M. L. Thompson (2009). "Use of combination therapy with a beta-blocker and milrinone in patients with advanced heart failure." [Ann Pharmacother](#) **43**(11): 1872-6. [PDF Full-Text](#)

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OBJECTIVE: To review the literature evaluating the clinical effects of combination therapy with a beta-blocker and milrinone in patients with severe heart failure (HF). **DATA SOURCES:** Literature was accessed through MEDLINE (1950-June 2009), PubMed (1966-June 2009), and International Pharmaceutical Abstracts (1970-June 2009), with combinations of the following terms: positive inotrope, milrinone, dobutamine, and beta-receptor blocker. In addition, reference citations from publications identified were reviewed. **STUDY SELECTION AND DATA EXTRACTION:** All articles that examined the effect of combination therapy with a beta-blocker and milrinone on clinical endpoints in patients with advanced HF were assessed. **DATA SYNTHESIS:** A search of the literature revealed 4 studies examining the clinical effects of combination therapy with a beta-blocker and milrinone. Three of these studies were retrospective reviews, while one was a post hoc subgroup analysis from the OPTIME-CHF study. Concomitant therapy with milrinone and a beta-blocker was well tolerated, with no significant increase in adverse events or deterioration in clinical status in any study. Tolerability rates for combination therapy ranged from 88% to 92%. In 2 of the studies, roughly 50% of the patients in the combination arm were able to be weaned off milrinone. One study suggested a mortality reduction in favor of combination therapy over milrinone alone, while another study suggested no difference in mortality with combination therapy versus milrinone monotherapy. One study suggested a potential increase in mortality when beta-blocker therapy was withdrawn in patients who were started on milrinone. None of the studies demonstrated any significant differences in hospitalization rates. All of the studies were limited by their retrospective nature and small sample size. **CONCLUSIONS:** Data are insufficient to make firm conclusions on the clinical benefit of combination therapy with a beta-blocker and milrinone in patients with advanced HF, although it appears that this regimen is well tolerated and may allow weaning of inotropic support.

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Pharmacy

Kalus, J. S. (2009). "Pharmacologic management of atrial fibrillation: established and emerging options." *J Manag Care Pharm* **15**(6 Suppl B): S10-8. [Article Request Form](#)

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BACKGROUND: In patients with atrial fibrillation (AF), antiarrhythmic drug therapy currently plays a greater role in maintaining sinus rhythm after cardioversion than it does in converting AF to sinus rhythm. Amiodarone is the most effective antiarrhythmic agent for maintaining sinus rhythm after cardioversion in patients with AF. However, its pharmacokinetics is complex; the drug interacts with many commonly used medications; and long-term use can cause thyroid dysfunction, hepatotoxicity, and other severe extracardiac adverse effects. The use of antiarrhythmic strategies in patients with AF has decreased because of evidence of greater safety and lower costs for hospitalization obtained from the use of rate-control strategies instead. Nevertheless, some patients require a rhythm-control strategy. Warfarin is used to prevent embolic stroke in many patients with AF, but its use is also complex and requires monitoring. Therefore, efforts have been made to develop antiarrhythmic agents with improved tolerability and anticoagulants that are easy to use. **OBJECTIVES:** To describe the 3 primary goals of pharmacotherapy in patients with AF, compare and contrast the efficacy and safety of established and investigational pharmacotherapies for AF, and recommend a drug regimen for an individual with AF based on patient-specific factors. **SUMMARY:** Currently available antiarrhythmic agents differ in their efficacy for maintaining sinus rhythm after cardioversion in AF patients with tolerability problems, comorbidities (particularly heart failure and renal impairment), and potential drug interactions. Hence, when selecting drug therapy to maintain sinus rhythm after cardioversion, it is important to take into consideration patient characteristics, including age, disease states, renal function, and concurrent drug therapies. Outpatient self-administration of single loading doses of flecainide or propafenone with what is referred to as the pill-in-the-pocket approach may be considered for carefully selected patients with recurrent episodes of symptomatic AF. The recently approved antiarrhythmic agent dronedarone has electrophysiologic properties similar to those of amiodarone, but its lack of iodine may improve upon the pharmacokinetic and tolerability issues associated with amiodarone. Vernakalant is another investigational antiarrhythmic agent that may prove useful for cardioversion and maintenance of sinus rhythm after cardioversion in patients with AF. New oral anticoagulants that do not require close laboratory monitoring and are simpler to use than warfarin have been used investigationally for prevention of venous thromboembolism and are in clinical trials for prevention of embolic stroke in patients with AF. **CONCLUSIONS:** Pharmacotherapy for patients with AF should be individualized based on patient-specific factors. New therapeutic options may become available to facilitate treatment of these patients.

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Pulmonary & Critical Care Medicine

Burke, R. R., I. M. Obeid, L. K. Williams and Z. Q. Morris (2009). "Two ATS recommended protocols for administration of methacholine are not equal." *J Asthma* **46**(7): 740-4. [Article Request Form](#)

Henry Ford Health System, Division of Pulmonary and Critical Care Medicine, Detroit, Michigan 48202, USA.

BACKGROUND: The 1999 American Thoracic Society methacholine challenge guidelines stated that the 5-breath dosimeter method of methacholine administration is similar to the 2-minute tidal breath method. Recent data has disputed this assertion. We examined the differences in the diagnosis of asthma using these two methods. **METHODS:** Data were abstracted from a prospectively generated pulmonary function database over 4 years. During the first 2 years the 5-breath dosimeter method was used, and the subsequent 2 years the 2-minute tidal breath method was used. The effect of the delivery technique was assessed by crude and adjusted odds ratios, controlling for known confounders and group differences. **RESULTS:** A total of 907 subjects underwent methacholine challenge testing during the 4-year study period: 19.3% of the subjects tested with the 5-breath dosimeter method and 31.2% of those tested with the 2-minute tidal breathing method had a PC₂₀ \leq 8.0 mg/mL (OR 1.90, 95% CI 1.4 to 2.58, $p < 0.001$). The ability to reliably exclude airway hyper-responsiveness (PC₂₀ $>$ 16.0 mg/mL) was also altered by the differences between the testing techniques. Using the 5-breath dosimeter method, 72.4% of subjects were ruled out for airway hyper-responsiveness, whereas only 59.9% of subjects were ruled out with the 2-minute tidal breathing technique ($p < 0.001$). **CONCLUSION:** The two recommended protocols for the diagnosis of asthma are not equivalent and significantly alter the rate of diagnosis of asthma as well as the severity. The differences were seen across all

PC20 levels, from those with strongly positive tests (PC20 \leq 1.0 mg/mL) as well as those with negative tests for airway hyper-responsiveness (PC20 > 16.0 mg/mL).

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Radiation Oncology

Corn, B. W., M. H. Wang, S. Fox, J. Michalski, J. Purdy, J. Simpson, J. Kresl, W. J. Curran, A. Diaz, M. Mehta and B. Movsas (2009). "Health related quality of life and cognitive status in patients with glioblastoma multiforme receiving escalating doses of conformal three dimensional radiation on RTOG 98-03." Journal of Neuro-Oncology **95**(2): 247-257. [PDF Full-Text](#)

[Corn, Benjamin W.] Tel Aviv Med Ctr & Sch Med, IL-64239 Tel Aviv, Israel. [Wang, Meihua] RTOG, Stat Unit, Philadelphia, PA USA. [Fox, Sherry] Cullather Brain Tumor QOL Ctr Bonsecours Richmond, Chesterfield, VA 23832 USA. [Michalski, Jeffrey] Washington Univ, Med Ctr, St Louis, MO 63110 USA. [Purdy, James] Univ Calif Davis, Med Ctr, Sacramento, CA 95817 USA. [Simpson, Joseph] Washington Univ, St Louis, MO 63110 USA. [Kresl, John] Arizona Oncol Serv, Phoenix, AZ 85013 USA. [Curran, Walter J., Jr.] Emory Univ, Sch Med, Atlanta, GA 30322 USA. [Diaz, Aidnag] Canc Therapy & Res Ctr S Texas, San Antonio, TX 78229 USA. [Mehta, Minesh] Univ Wisconsin, Sch Med & Publ Hlth, Madison, WI 53792 USA. [Movsas, Benjamin] Henry Ford Hosp, Detroit, MI 48202 USA.

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The Radiation Therapy Oncology Group (RTOG) embarked on a phase I/II study of patients suffering from glioblastoma multiforme (protocol 98-03) to assess the impact of dose escalation with 3-D conformal techniques. The primary endpoints were feasibility and survival. This report describes the outcome of secondary endpoints (quality of life and neurocognitive function). Patients with supratentorial GBM were treated with a combination of carmustine (BCNU) and conformal irradiation (dose levels: 66, 72, 78, 84 Gy, respectively). Quality of Life was assessed with the Spitzer Quality of Life Index. Neurocognitive function was determined by the Mini Mental Status Examination. The latter tests were administered at the start of irradiation, at the end of irradiation and then at 4 month intervals. Relatively high compliance was achieved with both of the tools (SQLI; MMSE). Overall rates of survival between baseline SQLI scores <7 and 7-10 were statistically significantly different [HR = 1.72, 95% CI (1.22, 2.4), P = 0.0015]. The significant impact of high SQLI score on survival was preserved in multivariate analysis. The component of this index which made the greatest contribution was the patient's independence. There was continual deterioration of neurocognitive function within the populations studied. No correlation was seen between dose escalation and the secondary endpoints studied. Radiation dose escalation and assessment of its impact on life quality and neurocognition can be carried out in a large international trial. Baseline SQLI is a statistically significant determinant of survival. Those who maintain independence have superior survival to those who are reliant on others.

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Radiation Oncology

Rao, S., A. Patel, K. Levin, M. Lu, K. Garbarino, D. Myers, E. M. Walker, S. Ryu, J. H. Kim and B. Movsas (2009). "How Often are Previously Undetected Radiographic Abnormalities Detected at the Time of CT Simulation for Breast Cancer Patients?" Am J Clin Oncol **EPub Ahead of Print**. [Article Request Form](#)

From the Departments of Radiation Oncology and Radiology, Henry Ford Hospital, Detroit, Michigan; and Department of Biostatistics and Research Epidemiology, Henry Ford Health System, Detroit, Michigan.

OBJECTIVES:: In most institutions, planning computed tomography (CT) scans are not interpreted by diagnostic radiologists. The purpose of this analysis was to determine the percentage of cases in which a previously undetected radiographic finding was found on review of CT simulation images by diagnostic radiology. **METHODS::** At the Henry Ford West Bloomfield Center, CT simulations are prospectively interpreted by diagnostic radiologists and a formal report is generated. CT simulation scan reports of 332 consecutive breast cancer patients from 2000 to 2006 were reviewed. The percentage of these reports in which a previously undetected abnormality was noted on the planning CT was determined. Prior and subsequent diagnostic CT scans were also reviewed to determine the clinical relevance of these diagnostic abnormalities. **RESULTS::** Of 332 patients with CT simulations for breast cancer treatment planning, 52 patients (16%) had a newly detected abnormality noted. Of these, 31 patients (or 60% of the abnormal

findings) were deemed by diagnostic radiology to have potentially significant findings (eg, "can not exclude metastatic disease"), and a follow-up CT or MRI scan was recommended. Abnormalities in this category included previously undetected lung nodules, liver lesions, kidney/adrenal lesions, and sclerotic bony lesions. On follow-up, however, to date, these findings have demonstrated no clinical significance, although further follow-up is needed in many patients. CONCLUSIONS:: In this study, a significant proportion of breast cancer patients undergoing CT planning studies were diagnosed with potential abnormalities for which follow-up was recommended by diagnostic radiology. To date, these findings have not been clinically relevant, though further follow-up is needed in many of the patients. Thus, in cases of clinical uncertainty, a diagnostic radiologist should be consulted and follow-up imaging obtained if necessary.

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Radiation Oncology

Siddiqui, F., A. Kolozsvary, K. N. Barton, S. O. Freytag, S. L. Brown and J. H. Kim (2009). "Does hyperthermia increase adenoviral transgene expression or dissemination in tumors?" Int J Hyperthermia **25**(4): 273-9. [Article Request Form](#)

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PURPOSE: Viral vectors used for cancer gene therapy are usually delivered by direct intratumoral administration. We studied the role of hyperthermia (HT) in vitro and in vivo in an attempt to achieve higher transfection rates (especially, larger volume of spread). **MATERIALS AND METHODS:** Replication-deficient adenoviruses containing either the human sodium-iodide symporter (Ad5-CMV-hNIS) or green fluorescent protein (Ad5-CMV-eGFP) as reporter genes were used. For in vitro studies, human lung cancer A549 cells were transfected with the virus and assayed for hNIS expression by radioactive pertechnetate uptake or green fluorescence activity using a gamma-counter or fluoroscopy respectively in the presence and absence of HT. For in vivo studies, A549 tumors were established intramuscularly in CD1 athymic mice. The adenoviral constructs (10(10) viral particles/tumor) were injected intratumorally when the tumors reached 10-11 mm in diameter. Different timing sequences of HT were examined and viral spread was assessed using technetium-autoradiography or GFP-fluorescence microscopy. **RESULTS:** In the in vitro studies, A549 cells infected with the adenoviral construct did not show any difference in gene expression level in the presence or absence of HT. In vivo, the effect of HT on the volume of gene expression in A549 tumors was highly variable with some groups of mice showing better spread in the presence of HT and others showing reduced spread with HT. **CONCLUSION:** Improvements in intratumoral adenoviral spread in response to hyperthermia were not consistently observed in a mouse tumor model using two quantitative endpoints of gene expression.

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Radiation Oncology

Zhong, H. L. and J. V. Siebers (2009). "Monte Carlo dose mapping on deforming anatomy." Physics in Medicine and Biology **54**(19): 5815-5830. [Article Request Form](#)

[Zhong, Hualiang; Siebers, Jeffrey V.] Virginia Commonwealth Univ, Dept Radiat Oncol, Richmond, VA 23298 USA. [Zhong, Hualiang] Henry Ford Hlth Syst, Dept Radiat Oncol, Detroit, MI 48202 USA.
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This paper proposes a Monte Carlo-based energy and mass congruent mapping (EMCM) method to calculate the dose on deforming anatomy. Different from dose interpolation methods, EMCM separately maps each voxel's deposited energy and mass from a source image to a reference image with a displacement vector field (DVF) generated by deformable image registration (DIR). EMCM was compared with other dose mapping methods: energy-based dose interpolation (EBDI) and trilinear dose interpolation (TDI). These methods were implemented in EGSnrc/DOSXYZnrc, validated using a numerical deformable phantom and compared for clinical CT images. On the numerical phantom with an analytically invertible deformation map, EMCM mapped the dose exactly the same as its analytic solution, while EBDI and TDI had average dose errors of 2.5% and 6.0%. For a lung patient's IMRT treatment plan, EBDI and TDI differed from EMCM by 1.96% and 7.3% in the lung patient's entire dose region, respectively. As a 4D Monte Carlo dose calculation technique, EMCM is accurate and its speed is comparable to 3D Monte Carlo simulation. This method may serve as a valuable tool for accurate dose accumulation as well as for 4D dosimetry QA.

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Sleep Medicine

Chhangani, B. S., T. A. Roehrs, E. J. Harris, M. Hyde, C. Drake, D. W. Hudgel and T. Roth (2009). "Pain sensitivity in sleepy pain-free normals." [Sleep](#) **32**(8): 1011-7. PMC2717191. [PDF Full-Text](#)

Sleep Disorders & Research Center, Henry Ford Health System, Detroit, MI 48202, USA.

STUDY OBJECTIVE: Past studies have shown that acute experimental reduction of time in bed in otherwise healthy, non-sleepy people leads to hyperalgesia. We hypothesized that otherwise healthy, sleepy people may also exhibit hyperalgesia relative to their non-sleepy counterparts. DESIGN: Between-groups sleep laboratory study. SETTING: Hospital-based sleep disorders center. PARTICIPANTS: Twenty-seven, healthy, normal participants (age 18-35 years) were recruited and categorized into sleepy and non-sleepy groups based on their average sleep latencies on a screening multiple sleep latency test (MSLT). INTERVENTIONS: Both groups were then allowed 8 hours time in bed, following which they underwent pain sensitivity testing (10:30 and 14:30) and sleepiness assessments by the MSLT (10:00, 12:00, 14:00, and 16:00). Pain sensitivity assessments were made by measuring finger withdrawal latencies to a radiant heat source delivering 5 different heat intensities. MEASUREMENTS AND RESULTS: This study showed that after only one night of 8 hours time in bed, the sleepy participants continued to be sleepy and exhibited a more rapid finger withdrawal response (i.e., increased pain sensitivity) to radiant heat than non-sleepy participants. CONCLUSION: This suggests that sleepy individuals experience hyperalgesia in response to a painful stimulus when compared with non-sleepy individuals.

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Sleep Medicine

Dement, W. C., R. D. Cartwright, T. Roth and J. C. Ware (2009). "Ismet (John) Karacan, M.D, D.Sc. OBITUARY." [Journal of Clinical Sleep Medicine](#) **5**(5): 486-487. [PDF Full-Text](#)

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Sleep Medicine

Khalid, I., L. Rana, T. J. Khalid and T. Roehrs (2009). "Refractory Restless Legs Syndrome Likely Caused by Olanzapine." [Journal of Clinical Sleep Medicine](#) **5**(1): 68-69. [PDF Full-Text](#)

[Khalid, Imran; Rana, Lopa; Khalid, Tabindeh J.; Roehrs, Timothy] Henry Ford Hlth Syst, Detroit, MI 48202 USA.

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We report a case of severe restless legs syndrome (RLS) that occurred as a side effect of olanzapine therapy. It was refractory to treatment with 2 mg of clonazepam and 3 mg ropinirole. There was partial relief with propoxyphene, however, it was stopped because of side effects. The symptoms disappeared once olanzapine was switched to another antipsychotic medication. Only two prior published reports associate olanzapine usage with development of RLS. In one report, low-dose benzodiazepines and ropinirole were associated with resolution of RLS symptoms stating dopamine depletion as the likely etiology. In our patient, however, RLS due to olanzapine was refractory to the trial of both high-dose benzodiazepine and ropinirole. This suggests that RLS occurring as a side effect of olanzapine therapy may have additional causative mechanisms beyond simple dopamine depletion as postulated before. High-dose narcotics, if tolerated, may be an alternative in such refractory cases.

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Sleep Medicine

Quadri, S., C. Drake and D. W. Hudgel (2009). "Improvement of Idiopathic Central Sleep Apnea with Zolpidem." Journal of Clinical Sleep Medicine 5(2): 122-129. [PDF Full-Text](#)

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Study Objectives: We hypothesized that the non-benzodiazepine hypnotic zolpidem would improve idiopathic central sleep apnea (ICSA) by enhancing sleep stability, resulting in fewer arousals, which in turn would lessen oscillation in arterial CO₂ and produce a decrease in central apnea/hypopnea events. Zolpidem might also decrease ventilatory control responsiveness during arousals, thereby reducing hyperpnea, hypocapnia, and subsequent apneas. **Patients and Study Design:** This was a case series in which all patients with ICSA seen in the Henry Ford Sleep Disorders Clinic from January 1, 2004, to December 31, 2006, were offered zolpidem, as well as other therapeutic options of acetazolamide, continuous positive airway pressure (CPAP), bilevel pressure support, or assist control ventilatory support. Those 20 patients who chose zolpidem were prescribed 10 mg at bedtime. **Measurements and Results:** After a therapeutic trial averaging 9 weeks, a follow-up polysomnogram showed that the overall apnea/hypopnea index (AHI) and central AHI (CAHI) decreased, 30.0 +/- 18.1 (SD) to 13.5 +/- 13.3 ($p = 0.001$), and 26.0 +/- 17.2 to 7.1 +/- 11.8 ($p < 0.001$), respectively, without an overall change in obstructive AHI or arterial oxygen saturation. The total number of arousals per hour decreased with zolpidem use, 24.0 +/- 11.6 to 15.1 +/- 7.7 ($p < 0.001$), leading to a significant improvement in sleep efficiency. There was a positive correlation between the decrease in CAHI and the arousal index. Consistent with the hypnotic effect of zolpidem, sleep latency decreased, stage 1 sleep percentage decreased, and stage 2 percentage increased (all significant), without changes in stage 3-4 or REM sleep. Excessive daytime sleepiness, measured by the Epworth Sleepiness Scale (ESS) decreased from 13 +/- 5 to 8 +/- 5 ($p < 0.001$). Three patients experienced a significant increase in obstructive events. **Conclusion:** In an open-label trial, ICSA patients studied experienced a decrease in central apnea/hypopneas with zolpidem. They also had improved sleep continuity and decreased subjective daytime sleepiness, without a worsening of oxygenation or obstructive events in the majority of patients. However, in the absence of a randomized, controlled trial, zolpidem cannot be recommended for treatment of ICSA at this time.

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Surgery

Deeb, D., X. Gao, H. Jiang, B. Janic, A. S. Arbab, Y. Rojanasakul, S. A. Dulchavsky and S. C. Gautam (2009). "Oleanane triterpenoid CDDO-Me inhibits growth and induces apoptosis in prostate cancer cells through a ROS-dependent mechanism." Biochem Pharmacol **EPub Ahead of Print**. [Article Request Form](#)

Department of Surgery, Henry Ford Health System, Detroit, MI, United States.

CDDO-Me, a synthetic triterpenoid derived from oleanolic acid, is a promising anticancer agent that has shown strong activity against a wide variety of cancer types in vitro and in vivo. We have previously shown that CDDO-Me induces apoptosis in prostate cancer cells irrespective of their hormonal status. To further understand the proapoptotic mechanism of CDDO-Me, we investigated the role of reactive oxygen species (ROS) in mediating the apoptosis inducing activity of CDDO-Me in LNCaP and PC-3 prostate cancer cell lines. Here, we show that CDDO-Me induces ROS generation from both nonmitochondrial and mitochondrial sources, which is associated with the induction of apoptosis as characterized by increased annexin V-binding, cleavage of PARP-1 and procaspases-3, -8, -9, loss of mitochondrial membrane potential and release of cytochrome c. In addition, CDDO-Me inhibited cell survival Akt, NF-kappaB and mTOR signaling proteins. The inhibition of ROS generation by N-acetylcysteine (NAC) or by overexpression of antioxidant enzymes glutathione peroxidase (GPx) and superoxide dismutase-1 (SOD-1) prevented CDDO-Me-induced apoptosis. Pretreatment with NAC blocked annexin V-binding, cleavage of PARP-1 and procaspases-3, -8, -9, loss of mitochondrial membrane potential and release of cytochrome c by CDDO-Me. NAC also prevented the inhibition of constitutively active Akt, NF-kappaB and mTOR by CDDO-Me. Together, these data indicate that ROS plays an essential role in the induction of apoptosis by CDDO-Me in prostate cancer cells.

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Surgery

Fregene, A., X. L. Jing, L. A. Monson and S. R. Buchman (2009). "Alteration in Volumetric Bone Mineralization Density Gradation Patterns in Mandibular Distraction Osteogenesis following Radiation Therapy." Plastic and Reconstructive Surgery **124**(4): 1237-1244. [PDF Full-Text](#)

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Background: The use of mandibular distraction osteogenesis for tissue replacement after oncologic resection or for deformations secondary to radiotherapy could have immense therapeutic ramifications. Radiotherapy, however, drastically impairs bone healing, potentially precluding the use of mandibular distraction osteogenesis as a durable reconstructive option. The authors have previously demonstrated significantly decreased mechanical and histologic metrics of the mandibular distraction osteogenesis regenerate after 36 Gy. The authors' goal is to now investigate the effect of these same radiation dosages on bone densitometrics using micro-computed tomographic scanning. Methods: Six Sprague-Dawley rats received 36-Gy fractionated radiotherapy sessions to the left mandible; six received none. All animals had external fixators placed, creation of osteotomies, distraction, and consolidation. Mandibles were scanned with micro-computed tomographic scanning. Volumetric density and microdensitometric measurements were analyzed. Results: There was a significant difference in volumetric bone mineralization patterns in irradiated animals. Bone volume fraction and bone mineral density, however, demonstrated no significant differences. Conclusions: The authors discovered a significant increase of low mineralized, immature bone and a significant decrease of highly mineralized, mature bone in the irradiated regenerate. These findings corroborate the authors' hypothesis that radiation induces a diminution in cell function, impairing optimal bone regeneration. Overall densitometrics, however, were unchanged according to micro-computed tomographic measurements, despite documented significant changes in biomechanical and histologic metrics. An optimal radiation dose must now be sought that demonstrates a higher degree of reproducible degradation, but not irreversible destruction, in all three outcomes. Such an approach will allow formulation of therapeutic interventions designed to enhance mandibular distraction osteogenesis so that it may be used as a viable reconstructive option. (*Plast. Reconstr. Surg.* 124: 1237, 2009.)

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Surgery

Gao, X. H., D. Deeb, Y. B. Liu, S. Gautam, S. A. Dulchavsky and S. C. Gautam (2009). "Immunomodulatory activity of xanthohumol: inhibition of T cell proliferation, cell-mediated cytotoxicity and Th1 cytokine production through suppression of NF-kappa B." Immunopharmacology and Immunotoxicology **31**(3): 477-484. [Article Request Form](#)

[Gao, Xiaohua; Deeb, Dorrah; Liu, Yongbo; Gautam, Sarita; Dulchavsky, Scott A.; Gautam, Subhash C.] Henry Ford Hlth Syst, Dept Surg, Div Surg Res, Detroit, MI 48202 USA.
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Xanthohumol (XN), a prenylated chalcone present in hops (*Humulus lupulus* L.) and beer, exhibits anti-inflammatory, antioxidant and anti proliferative activity, but has not been studied for effects on T cell-mediated immune responses. Here we demonstrate that XN has profound immunosuppressive effects on T cell proliferation, development of IL-2 activated killer (LAK) cells, cytotoxic T lymphocytes (CTLs), and production of Th1 cytokines (IL-2, IFN-gamma and TNF-alpha). The suppression of these cell-mediated immune responses by XN was at, least in part, due to the inhibition of nuclear factor kappa B (NF-kappa B) transcription factor through suppression of phosphorylation of I kappa B alpha, an inhibitor of NF-kappa B.

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Surgery

Joseph, B., J. M. Morton, T. Hernandez-Boussard, I. Rubinfeld, C. Faraj and V. Velanovich (2009). "Relationship Between Hospital Volume, System Clinical Resources, and Mortality in Pancreatic Resection." Journal of the American College of Surgeons **208**(4): 520-527. [PDF Full-Text](#)

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BACKGROUND: The relationship between hospital volume and perioperative mortality in pancreaticoduodenectomy has been well established. We studied whether associations exist between hospital volume and hospital clinical resources and between both of these factors to mortality to help explain this relationship. **STUDY DESIGN:** This two-part study reviewed publicly available hospital information from the Leapfrog Group, HealthGrades, and hospital Web sites. Hospitals were evaluated for Leapfrog ICU staffing criteria and Safe Practice Score; HealthGrades five-star rating for complex gastrointestinal procedures and operations; and presence of a general surgery residency, gastroenterology fellowship, and interventional radiology. Evaluation used trend analysis and multiple logistic regression analysis. The second part determined the mortality rate for pancreaticoduodenectomy using inpatient mortality data from the National Inpatient Sample and Leapfrog. Hospitals were categorized by low volume (≤ 10 /year), high volume (≥ 11 /year), strong clinical support (presence of all support factors), and weak clinical support (absence of any factor). Data were correlated by number of pancreatic resections per hospital, hospital system clinical resources, and operative mortality. **RESULTS:** As hospital volume increased, statistically significant increases occurred in the frequency of hospitals meeting Leapfrog ICU staffing criteria ($p < 0.0001$), Leapfrog Safe Practice Score ($p = 0.0004$), HealthGrades 5-star rating ($p < 0.00001$), general surgery residency ($p < 0.00001$), gastroenterology fellowship ($p < 0.00001$), and interventional radiology services ($p < 0.00001$). No significant relationships were found between resection volume and any one of the clinical support factors and perioperative death. Presence of strong clinical support was associated with lower mortality (odds ratio = 0.32; $p = 0.001$). **CONCLUSIONS:** System clinical resources were more influential in operative mortality for pancreatic resection. This might help explain why high-volume hospitals, low-volume surgeons in high-volume institutions, and some lower-volume hospitals with excellent clinical resources have lower perioperative mortality rates for pancreatic resection. (J Am Coll Surg 2009;208:520-527. c 2009 by the American College of Surgeons)

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Surgery

Otto, C., D. R. Hamilton, B. D. Levine, C. Hare, A. E. Sargsyan, P. Altshuler and S. A. Dulchavsky (2009). "Into Thin Air: Extreme Ultrasound on Mt Everest." Wilderness & Environmental Medicine **20**(3): 283-289. [Article Request Form](#)

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Objective.-Mountaineers face a variety of health risks at altitude including pulmonary edema; portable ultrasound may be used to diagnose high altitude pulmonary edema. This report tests the functionality of electronic equipment in it hypobaric test environment and the ability of remotely guided nonexperts to use ultrasound to evaluate respiratory status on Mt Everest. **Methods.**-Two ultrasound devices and associated video equipment were tested in a cooled (4 degrees C-5 degrees C) hypobaric chamber to 27 000 feet (8230 m) before travel to Mt Everest. The ultrasound system was connected via satellite phone to a video streaming device and portable computer to stream video through the Internet for remote guidance of a novice user by an expert. Pulmonary interstitial fluid was quantified by the presence of "comet tail" artifacts. **Results.**-There was no notable degradation in equipment performance in cold, hypobaric conditions; ultrasound confirmation of increased comet tails was noted in the chamber despite oxygen supplemental ion and the very brief exposure. Two pulmonary surveys of asymptomatic participants were completed by novice operators within 25 minutes on Mt Everest. The remote expert was able to guide and identify comet tails Suggestive of intermediate Pulmonary interstitial fluid. Image quality was excellent. **Conclusions.**-The tested ultrasound devices functioned nominally in cold, hypobaric conditions; acute changes in lung fluid content were noted in these conditions despite normoxia. We successfully used a satellite telemedical connection with a remote expert to guide thoracic ultrasound examinations at Advanced Base Camp on Mt Everest. Coupling portable ultrasound with remote expert guidance telemedicine provides a robust diagnostic capability in austere locations.

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Surgery

Velanovich, V. (2009). "Difficulty in assessing quality of life outcomes in a fluctuating disease: a hypothesis based on gastroparesis." Gastroenterol Res Pract **2009**: 396190. PMC2762185. [PDF Full-Text](#)

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An underlying assumption of quality of life outcome research is that after some intervention a "steady-state" of quality of life is reached which can be identified as an endpoint, and, hence, the "outcome." However, in some disease processes, no such steady-state is reached. The hypothesis presented is that a disease process with a waxing and waning course will make it difficult to determine a quality of life endpoint. After clinical observation, a pilot study of patients with either diabetic or idiopathic gastroparesis with gastric neurostimulation their records were reviewed to identify the number of clinic visits, the number of clinic visits in which the patients were asymptomatic, much improved, improved, no change, worse, or much worse. These changes were defined as "transitions." A "transition ratio" was calculated by dividing the number of transitions by the number of clinic visits. Preliminary results showed that of 32 patients, the median number of clinic encounters was 8 (1-35), and the median number of transitions 4 (0-22). The average transition ration was 0.56 +/- 0.31. In the case of gastroparesis, over half of all clinical encounters were associated with a transition. The implication of the hypothesis and preliminary finding suggests a difficulty to identify when the symptomatic endpoint was reached. Other methods to assess the effects of treatment in such a disease process are required to fully understand the effects of treatment on quality of life.

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Surgery

Velanovich, V. (2009). "Endoscopic endoluminal radiofrequency ablation of Barrett's esophagus: initial results and lessons learned." Surgical Endoscopy and Other Interventional Techniques **23**(10): 2175-2180. [Article Request Form](#)

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Background Ablating Barrett's epithelium may reduce the risk of developing esophageal adenocarcinoma. This study reports the experience of a single surgeon using an endoscopic endoluminal device that delivers radiofrequency energy (the BARRx device) to ablate Barrett's esophagus. Methods All patients who underwent ablation of Barrett's epithelium with the BARRx system were reviewed for length of Barrett's metaplasia, presence of high-grade dysplasia, postprocedure complications, completeness of ablation at first follow-up endoscopy, need for additional ablation, completeness of ablation at second follow-up endoscopy, and concomitant performance of a Nissen fundoplication. Results Sixty-six patients underwent Barrett's ablation. The median length of the Barrett's esophagus was 3 (range, 1-14) cm. Twelve patients (18%) had high-grade dysplasia. There were no immediate procedure-related complications. Four strictures occurred: three in patients with \geq 12-cm segments of Barrett's and one in a 6-cm segment. Twenty-nine of 49 patients (59%) who had planned 3-month follow-up endoscopy had complete ablation. Five patients had planned two-stage ablation. Twenty patients with incomplete ablation had additional ablation. Twenty-seven patients had planned follow-up endoscopy at \geq 1 year: 25 of 27 (93%) had biopsy-proven normal esophageal mucosa. The median length of Barrett's esophagus in patients with initially incomplete ablation was 6 cm, compared with 2 cm in the initially complete ablation patients. Seven Nissen funduplications were present at the time of ablation, whereas six were performed concomitantly with the ablation without increased difficulty. Conclusions Complete ablation of Barrett's esophagus with radiofrequency endoluminal ablation is achievable in $>90\%$ of patients. Patients with longer segments are likely to require additional ablation. Patients with very long segments are at risk for stricture and should be approach cautiously. Performance of a fundoplication is not hindered by concomitant ablation.

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Urology

Diaz, M. (2009). "Predictive Factors for Vesicoureteral Reflux and Prenatally Diagnosed Renal Pelvic Dilatation COMMENT." Journal of Urology **182**(5): 2445-2445. [PDF Full-Text](#)

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Urology

Krane, L. S., C. Wambi, A. Bhandari and H. J. Stricker (2009). "Posterior support for urethrovesical anastomosis in robotic radical prostatectomy: single surgeon analysis." Canadian Journal of Urology **16**(5): 4836-4840. [Article Request Form](#)

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Introduction: Posterior urethrovesical anastomotic support has been reported to improve early return of urinary continence following radical prostatectomy. We adapted this technique to evaluate enhancement of early urinary control in patients undergoing robotic radical prostatectomy. Materials and methods: Forty-two consecutive men undergoing radical prostatectomy by a single surgeon between September and December 2007 received a posterior urethrovesical supporting stitch prior to the standard urethrovesical anastomosis (group 1). Operative data, postoperative complications, and follow up data were compared with those of the 42 consecutive men who underwent robotic radical prostatectomy by the same surgeon between March and August 2007 with a standard urethrovesical anastomosis (group 2). Continence was assessed at routine follow up visit 6 to 8 weeks following catheter removal. Continence was defined as zero pads or small security liner for infrequent urinary leakage in 24 hours. Results: Thirty-four (81%) and 37 (88%) men in groups 1 and 2 respectively had follow up available between 45 and 75 days following prostatectomy. Preoperative demographics were similar between the two groups. At a mean follow up of 60 and 53 days following surgery, 29/34 (85%) of men in group 1 and 32/37 (86%) of men in group 2 were continent. On multivariate logistic regression analysis, no factors were associated with improved continence between the two groups. Conclusions: Posterior urethrovesical anastomotic support did not result in improved early urinary control following radical prostatectomy. Excellent urinary control can be achieved in the patients undergoing robotic radical prostatectomy without posterior urethrovesical anastomotic support.

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Urology

Menon, M. (2009). "Extr fascial Versus Interfascial Nerve-sparing Technique for Robotic-assisted Laparoscopic Prostatectomy: Comparison of Functional Outcomes and Positive Surgical Margins Characteristics EDITORIAL COMMENT." Urology **74**(3): 616-616. [PDF Full-Text](#)

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Urology

Siddiqui, S. A., I. Frank, J. C. Cheville, C. M. Lohse, B. C. Leibovich and M. L. Blute (2009). "Postoperative surveillance for renal cell carcinoma: a multifactorial histological subtype specific protocol." BJU Int **104**(6): 778-85. [PDF Full-Text](#)

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OBJECTIVE: To create a model that adjusts surveillance after surgery to the natural history of surgically treated renal cell carcinoma (RCC), and to assess the cost of several surveillance models with a long-term longitudinal follow-up, as although there are many models for predicting the outcome in RCC, most surveillance protocols remain based primarily on stage alone, and thus might be inaccurate as they do not incorporate many other pathological features that have a significant effect on recurrence. PATIENTS AND

METHODS: We identified 1864, 357 and 118 patients with pM0 clear cell, papillary and chromophobe RCC, respectively, who had a radical or partial nephrectomy between 1970 and 2000. All recurrences were classified according to location (abdomen, thorax, bone, brain). Cox proportional hazards models were used to determine which pathological features were independently predictive of recurrence in each group. Three subtype-specific protocols were devised based on site-specific recurrence rates. **RESULTS:** Positive surgical margins, the 2002 Tumour-Node-Metastasis classification, size, nuclear grade, and histological tumour necrosis were independently associated with abdominal recurrence in patients with clear-cell RCC. These same features, except for surgical margins, were significantly associated with thoracic recurrence. The 2002 classification and nuclear grade were independently associated with abdominal and thoracic recurrence in patients with papillary RCC. No multivariate analysis was done for chromophobe RCC as there were only 10 recurrences to the abdomen and three to the thoracic region. However, these patients were stratified according to stage and grade, as recurrences in this group had a clear stage- and grade-specific pattern. **CONCLUSIONS:** We present a subtype-specific multifactorial surveillance protocol based on significant predictors of recurrence. This protocol is better than algorithms based on stage alone and can be used to effectively tailor postoperative imaging to the individual patient.

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Urology

Sivanandam, A., S. Siva and M. Bhandari (2009). "Re: Urethral Stricture is Now an Open Surgical Disease." Journal of Urology **182**(5): 2535-2536. [PDF Full-Text](#)

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