

Henry Ford Health System Publication List July 2009

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Biostatistics & Research Epidemiology

Beebe-Dimmer, J. L., N. L. Nock, C. Neslund-Dudas, A. Rundle, C. H. Bock, D. L. Tang, M. Jankowski and B. A. Rybicki (2009). "Racial Differences in Risk of Prostate Cancer Associated With Metabolic Syndrome." *Urology* **74**(1): 185-190. [PDF Full-Text](#)

[Beebe-Dimmer, Jennifer L.] Wayne State Univ, Barbara Ann Karmanos Canc Inst, Prentis Ctr, Detroit, MI 48201 USA. Wayne State Univ, Dept Internal Med, Sch Med, Detroit, MI 48201 USA. Case Western Reserve Univ, Dept Epidemiol & Biostat, Cleveland, OH 44106 USA. Henry Ford Hosp, Dept Biostat & Res Epidemiol, Detroit, MI 48202 USA. Columbia Univ, Dept Epidemiol, Mailman Sch Publ Hlth, New York, NY USA. Columbia Univ, Dept Environm Hlth Sci, Mailman Sch Publ Hlth, New York, NY USA.

Beebe-Dimmer, JL, Wayne State Univ, Barbara Ann Karmanos Canc Inst, Prentis Ctr, 110 E Warren Ave, 1115, Detroit, MI 48201 USA.

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OBJECTIVES To perform a case-control study to test the association between metabolic syndrome features and prostate cancer. The metabolic syndrome refers to a cluster of conditions serving as risk factors for cardiovascular disease. The metabolic syndrome is prevalent in the United States, and the spectrum of specific features has been shown to differ by race and ethnicity. A number of recent reports have linked metabolic syndrome to prostate cancer; however, Most Studies have not had racially diverse populations to explore differences in risk. **METHODS** A case-control study was conducted to test the association between metabolic syndrome features and prostate cancer among 637 patients and 244 controls, with African-American men constituting 43% of the study population. **RESULTS** Metabolic syndrome, defined using a modified version of the Adult Treatment Panel III criteria, was marginally associated with an increased risk of prostate cancer in African-American men (odds ratio [OR] 1.71, 95% confidence interval [CI] 0.97-3.01), but not in white men (OR 1.02, 95% CI 0.64-1.62). After stratifying the patients by stage at diagnosis, African-American men with organ-confined disease were more likely to have a history of metabolic syndrome than were the controls (OR 1.82; 95% CI 1.02-3.23), but no association was observed among those with advanced-stage disease (OR 0.93; 95% CI 0.31-2.77). When evaluating the specific features of the metabolic syndrome, obesity was inversely related to prostate cancer among white men (OR 0.51, 95% CI 0.33-0.80) but unrelated to risk among African-American men (OR 1.15, 95% CI 0.70-1.89). **CONCLUSIONS** In the present investigation, the metabolic syndrome was associated with prostate cancer risk in African-American men, but not in white men. The

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8:30am-5:00pm F

prevalence of this syndrome, Coupled with the racial disparity in prostate cancer incidence and outcomes after diagnosis, warrant additional investigation.

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Biostatistics & Research Epidemiology

McBride, C. M., S. H. Alford, R. J. Reid, E. B. Larson, A. D. Baxevasis and L. C. Brody (2009). "Characteristics of users of online personalized genomic risk assessments: Implications for physician-patient interactions." Genet Med. EPub Ahead of Print. [Article Request Form](#)

From the Social and Behavioral Research Branch, National Human Genome Research Institute, National Institutes of Health, Bethesda, Maryland; The Department of Biostatistics and Research Epidemiology, Henry Ford Health System, Detroit, Michigan; Group Health Cooperative, Center for Health Studies, Seattle, Washington; and Genome Technology Branch, National Human Genome Research Institute, National Institutes of Health, Bethesda, Maryland.

PURPOSE:: To evaluate what psychological and behavioral factors predict who is likely to seek SNP-based genetic tests for multiple common health conditions where feedback can be used to motivate primary prevention. **METHODS::** Adults aged 25-40 years who were enrolled in a large managed care organization were surveyed. Those eligible could log on to a secure study Web site to review information about the risks and benefits of a SNP-based genetic test and request free testing. Two primary outcomes are addressed: accessing the Web (yes or no) and deciding to be tested (completed a blood draw at the clinic) **RESULTS::** Those considering genetic susceptibility testing did not hold genetically deterministic beliefs (0.42 on scale of 0 [behavior] to 1 [genetic]) but believed genetic information to be valuable and were confident they could understand such information. Individuals who believed it important to learn about genetics (odds ratio = 1.28), were confident they could understand genetics (odds ratio = 1.26), and reported the most health habits to change (odds ratio = 1.39) were most likely to get tested. **CONCLUSIONS::** Individuals who present to health care providers with online genetics information may be among the most motivated to take steps toward healthier lifestyles. These motives might be leveraged by health care providers to promote positive health outcomes.

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Biostatistics & Research Epidemiology

Nock, N. L., C. Bock, C. Neslund-Dudas, J. Beebe-Dimmer, A. Rundle, D. Tang, M. Jankowski and B. A. Rybicki (2009). "Polymorphisms in glutathione S-transferase genes increase risk of prostate cancer biochemical recurrence differentially by ethnicity and disease severity." Cancer Causes Control. EPub Ahead of Print. [PDF Full-Text](#)

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OBJECTIVE: Genetic polymorphisms that modify the detoxifying activity of glutathione S-transferases (GSTs) can affect the level of carcinogenic metabolites created by endogenous steroid hormones and exogenous chemical substances. Although the GSTM1 null genotype has been shown to increase prostate cancer mortality in Caucasians, potential associations between GST polymorphisms and prostate cancer biochemical recurrence (BCR) have not been well studied, particularly in African-Americans. **METHODS:** We examined potential associations between the GSTM1 null, GSTT1 null and GSTP1 Ile105Val polymorphisms and BCR, after prostatectomy, in 168 African-American and 226 Caucasian patients treated at Henry Ford Hospital in Detroit, Michigan using Cox proportional hazards modeling. **RESULTS:** We found that African-Americans with the GSTT1 null genotype had increased BCR risk compared to those having GSTT1 present (hazard ratio (HR) = 2.30; 95% CI = 1.01-5.18; p = 0.04); and African-Americans with the GSTT1 null genotype and high grade tumors had an even greater risk (HR = 7.82; 95% CI = 2.49-24.50; p < 0.001). In Caucasians, an increased risk was observed in those patients with high grade tumors and the GSTM1 null genotype (HR = 2.88; 95% CI = 1.16-7.14; p = 0.02). Similar associations were observed for advanced stage and more aggressive (high grade or advanced stage) disease. **CONCLUSION:** Our results suggest GSTs may hold promise as therapeutic targets in more advanced prostate cancers, particularly, in African-Americans.

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Biostatistics & Research Epidemiology

Resnicow, K., R. Davis, N. Zhang, D. Tolsma, J. Calvi, G. Alexander, J. P. Anderson, C. Wiese and W. E. Cross (2009). "Tailoring a Fruit and Vegetable Intervention on Ethnic Identity: Results of a Randomized Study." *Health Psychology* **28**(4): 394-403. [Article Request Form](#)

[Resnicow, Ken] Univ Michigan, Sch Publ Hlth, Dept Hlth Behav & Hlth Educ, Ann Arbor, MI 48109 USA. [Tolsma, Dennis; Calvi, Josephine] Kaiser Permanente Georgia, Ctr Hlth Res SE, Atlanta, GA USA. [Alexander, Gwen] Henry Ford Hosp, Detroit, MI 48202 USA. [Cross, William E., Jr.] CUNY, Dept Psychol, New York, NY USA. Resnicow, K, Univ Michigan, Sch Publ Hlth, Dept Hlth Behav & Hlth Educ, 109 Observ St, Room 3867, SPH 1, Ann Arbor, MI 48109 USA. kresnic@umich.edu

Objective: Many targeted interventions have been developed and tested with African Americans (AA); however, AAs are a highly heterogeneous group. One characteristic that varies across AAs is Ethnic Identity (EI). Little research has been conducted on how to incorporate EI into the design of health messages and programs. Design: We tested whether tailoring a print-based fruit and vegetable (F & V) intervention on EI would enhance program impact. AA adults were recruited from two integrated healthcare delivery systems and then randomized to receive three newsletters focused on F & V behavior change over three months. One set of newsletters was tailored only on demographic and social cognitive variables (control condition), whereas the other (experimental condition) was additionally tailored on EI. Main Outcome Measures: The primary outcome for the study was F & V intake, assessed at baseline and three months later using the composite of two brief self-report frequency measures. Results: A total of 560 eligible participants were enrolled, of which 468 provided complete 3-month follow-up data. The experimental group increased their daily mean F & V intake by 1.1 servings compared to .8 servings in the control group ($p = .13$). Afrocentric experimental group participants showed a 1.4 increase in F & V servings per day compared to a .43 servings per day increase among Afrocentric controls ($p < .05$). Conclusions: Although the overall between-group effects were not significant, tailoring dietary messages on ethnic identity may improve intervention impact for some AA subgroups.

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Biostatistics & Research Epidemiology

Tolsma, D., J. Calvi, R. E. Davis, G. Alexander, S. M. Greene, C. Wiese, J. Anderson and K. Resnicow (2009). "Challenges in Researching Racially Sensitive Topics in HMOs." *Health Psychology* **28**(4): 389-390. [Article Request Form](#)

[Calvi, Josephine] Kaiser Permanente Georgia, Ctr Hlth Res SE, Piedmont Ctr 10, Atlanta, GA USA. [Davis, Rachel E.; Resnicow, Ken] Univ Michigan, Ctr Hlth Commun Res, Ann Arbor, MI 48109 USA. [Alexander, Gwen] Henry Ford Hlth Syst, Dept Biostat & Res Epidemiol, Detroit, MI USA. [Greene, Sarah M.; Wiese, Cheryl; Anderson, Julia] Grp Hlth, Ctr Hlth Studies, Seattle, WA USA. Calvi, J, Kaiser Permanente Georgia, Ctr Hlth Res SE, Piedmont Ctr 10, Atlanta, GA USA. josephine.calvi@kp.org

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Bone & Joint Center

Ciarelli, T. E., C. Tjhia, D. S. Rao, S. Qiu, A. M. Parfitt and D. P. Fyhrie (2009). "Trabecular packet-level lamellar density patterns differ by fracture status and bone formation rate in white females." *Bone*. Epub Ahead of Print. [PDF Full-Text](#)

Bone and Joint Center, Department of Orthopaedic Surgery, Henry Ford Hospital, Detroit, MI, USA.

Spatial patterns of mineralization for human iliac crest cancellous bone were measured from images obtained by quantitative backscattered electron microscopy. Biopsies collected from vertebral fracture patients and healthy individuals with high or low bone formation rate (BFR(s)) were examined (fracture/low BFR(s): N=12, fracture/high BFR(s): N=10, normal/low BFR(s): N=12, normal/high BFR(s): N=15). 20 by 20 pixel square areas or smaller were sampled from superficial and deep remodeling packets. Mean ($Z(\text{mean})$) and standard deviation (SD) of mineralization were measured, and coefficients of variation ($CV=SD/Z(\text{mean})$) were calculated. Fast Fourier transform analysis was used to quantify the distribution of the mineral in the packets. "FFT_ratio" was defined as the ratio magnitude of the principal spatial frequency to the average atomic number density. A higher FFT_ratio occurred in specimens with more pronounced alternating layers of light and dark as visible in the backscattered electron image, which was defined as lamellar patterning. Two-way ANOVA revealed that the coefficients of variation of mineralization for both superficial and deep packets were significantly lower in fracture patients than in normal individuals. However, the interaction between turnover rate and group (fracture/non-fracture) indicated that

the difference in packet CV occurred among the low turnover individuals and not among those with high turnover. Mean mineralization levels and CV between deep and superficial packets were highly correlated. Regressions of packet CV of mineralization and FFT_ratio were highly significant ($p < 0.001$) for all packets pooled and for packets divided by group (fracture/normal). However, analyses of packet CV and FFT_ratio by individual were variable (R^2 from 0.00338 to 0.700). Packet-level mineralization variability may be associated with fracture toughness, and fracture patients had less variable packet-level mineralization. The result that the packet CV varied significantly between fracture and non-fracture individuals with low turnover suggests that for low turnover subjects without fracture, high variability in mineralization may have a protective effect. In high turnover patients, the accelerated turnover may prevent the lamellar variability from developing over time. Strong correlations between CV and Z(mean) for both superficial and deep packets imply that newly formed bone is created similarly to older bone within an individual. Fourier transform results show that the mineralization variability found within packets is associated with lamellar patterning. Lamellar structure has been hypothesized to guide microcrack propagation in order to optimize bone strength and toughness. Osteoporotics with fracture had less pronounced lamellation than healthy normals and may be more prone to fracture.

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Cardiology

Chandra, A., S. W. Glickman, F. S. Ou, W. F. Peacock, J. K. McCord, C. B. Cairns, E. D. Peterson, E. M. Ohman, W. B. Gibler and M. T. Roe (2009). "An Analysis of the Association of Society of Chest Pain Centers Accreditation to American College of Cardiology/American Heart Association Non-ST-Segment Elevation Myocardial Infarction Guideline Adherence." Annals of Emergency Medicine **54**(1): 17-25. [PDF Full-Text](#)

[Chandra, Abhinav; Glickman, Seth W.] Duke Univ, Med Ctr, Durham, NC 27710 USA. [Ou, Fang-Shu; Peterson, Eric D.; Ohman, E. Magnus; Roe, Matthew T.] Duke Clin Res Inst, Durham, NC USA. [Peacock, W. Frank] Cleveland Clin, Cleveland, OH 44106 USA. [McCord, James K.] Henry Ford Hosp, Henry Ford Heart & Vasc Inst, Detroit, MI 48202 USA. [Cairns, Charles B.] Univ N Carolina, Chapel Hill, NC USA. [Gibler, W. Brian] Univ Cincinnati, Coll Med, Cincinnati, OH USA.
Chandra, A, Duke Univ, Med Ctr, Box 3096, Durham, NC 27710 USA. abhinav.chandra@duke.edu

Study objective: Since 2003, the Society of Chest Pain Centers (SCPC) has provided hospital accreditation for acute coronary syndrome care processes. Our objective is to evaluate the association between SCPC accreditation and adherence to the American College of Cardiology/American Heart Association (ACC/AHA) evidence-based guidelines for non-ST-segment elevation myocardial infarction (NSTEMI). The secondary objective is to describe the clinical outcomes and the association with accreditation. Methods: We conducted a secondary analysis of data from patients with NSTEMI enrolled in the Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes With Early Implementation of the ACC/AHA Guidelines (CRUSADE) quality improvement initiative in 2005. The analysis explored differences between SCPC-accredited and nonaccredited hospitals in evidence-based therapy given within the first 24 hours (including aspirin, beta-blocker, glycoprotein IIb/IIIa inhibitors, heparin, and ECG within 10 minutes). Results: Of 33,238 patients treated at 21 accredited hospitals and 323 nonaccredited hospitals, those at SCPC-accredited centers ($n=3,059$) were more likely to receive aspirin (98.1% versus 95.8%; odds ratio [OR] 1.73; 95% confidence interval [CI] 1.06 to 2.83) and beta-blockers (93.4% versus 90.6%; OR 1.68; 95% CI 1.04 to 2.70) within 24 hours than patients at non-SCPC-accredited centers ($n=30,179$). No difference was observed in obtaining a timely ECG (40.4% versus 35.2%; OR 1.28; 95% CI 0.98 to 1.67), administering a glycoprotein IIb/IIIa inhibitor (OR 1.30; 95% CI 0.93 to 1.80), or administering heparin (OR 1.12; 95% CI 0.74 to 1.70). Also, there was no significant difference in risk-adjusted mortality for patients treated at SCPC hospitals versus nonaccredited hospitals (3.4% versus 3.5%; adjusted OR 1.17; 95% CI 0.88 to 1.55). Conclusion: SCPC-accredited hospitals had higher NSTEMI ACC/AHA evidence-based guideline adherence in the first 24 hours of care on 2 of the 5 measures. No difference in outcomes was observed. Further studies are needed to better understand the association between SCPC accreditation and improved care for patients with acute coronary syndrome. [Ann Emerg Med. 2009;54:17-25.]

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Cardiology

Lemaitre, V., H. E. Kim, M. Forney-Prescott, Y. Okada and J. D'Armiento (2009). "Transgenic expression of matrix metalloproteinase-9 modulates collagen deposition in a mouse model of atherosclerosis." Atherosclerosis **205**(1): 107-112. [Article Request Form](#)

[Lemaitre, Vincent; Kim, Henry E.; D'Armiento, Jeanine] Columbia Univ, Coll Phys & Surg, Dept Med, Div Mol Med, New York, NY 10032 USA. [Kim, Henry E.] Henry Ford Hosp, Detroit, MI 48202 USA. [Forney-Prescott, Margaret] Novartis Pharmaceut, E Hanover, NJ USA. [Okada, Yasunori] Keio Univ, Dept Pathol, Tokyo, Japan. D'Armiento, J, Columbia Univ, Coll Phys & Surg, Dept Med, Div Mol Med, 630 W 168th St, P&S 8-401, New York, NY 10032 USA. jmd12@columbia.edu

Matrix metalloproteinase-9 (MMP-9) has been proposed to be an important modulator of atherosclerotic plaque vulnerability. We generated a transgenic (tg) model expressing human proMMP-9 in macrophages, using the scavenger receptor enhancer/promoter A. This model was crossed into the double Apoe/Timp-1 knockout background. After 16 weeks of a high-fat diet, there were no significant changes in plaque size in the proximal aortas between the four groups of the study population (Apoe(-/-), Apoe(-/-)/MMP-9tg, Apoe(-/-)/Timp-1(-/-), and Apoe(-/-)/MMP-9tg/Timp-1(-/-)), and, in the Timp-1 knockout background, MMP9 transgenic mice and control littermates had similar micro-aneurysm formation. However, lesions in Apoe(-/-)/MMP-9tg/Timp-1(-/-) mice contained significantly more collagen compared to the three other groups (P<0.005). Culture supernatants from elicited Apoe(-/-)/MMP-9tg/Timp-1(-/-) macrophages contained higher levels of active TGF-beta than the three other groups (P<0.05), suggesting that augmented collagen deposition resulted from an increase in TGF-beta activation due to transgenic MMP-9 in the Timp-1(-/-) background. This study indicates that, in human atherosclerosis, increased MMP-9 activity could up-regulate collagen deposition, possibly through TGF-beta activation. (C) 2008 Elsevier Ireland Ltd. All rights reserved.

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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." J Cardiopulm Rehabil Prev. Epub Ahead of Print. [Article Request Form](#)

RehabCare Group, St Louis, Missouri, and Department of Cardiac Health and Rehabilitation, Saint Thomas Hospital, Nashville, Tennessee (Dr Palevo); Division of Cardiovascular Medicine, Henry Ford Hospital, Detroit, Michigan (Dr Keteyian); and Department of Health and Human Performance, Middle Tennessee State University, Murfreesboro, Tennessee (Drs Kang and Caputo).

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 (10 patients) performed 24 ST exercise sessions (3 per week, 8 weeks), while the usual care (6 patients) group followed routine medical care. The structured isotonic ST program involved 12 different exercises on circuit weight machines. LV function (3D 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 LV 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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Center for Health Services Research

Burack, R. and J. E. Lafata (2009). "The Cost of Health Care Services Provided to Women Enrolled in a Community-Based Breast and Cervical Cancer Screening Program." Journal of Health Care for the Poor and Underserved **20(3)**: 713-720. [Article Request Form](#)

[Burack, Robert] Wayne State Univ, Dept Internal Med, Univ Hlth Ctr 5C, Detroit, MI 48201 USA. [Burack, Robert] Karmanos Canc Inst, Detroit, MI USA. [Lafata, Jennifer Elston] Henry Ford Hlth Syst, Ctr Hlth Serv Res, Detroit, MI USA.

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The National Breast and Cervical Cancer Early Detection Program (NBCCEDP) is a state-federal partnership that provides breast and cervical cancer-related services for low-income women but does not address other health care needs. We describe the annual cost and reimbursement associated with all services delivered to 483 program

enrollees at one health care system during 2001-03. The average per-enrollee cost for all clinical services provided was \$1,056. However, average revenue was \$533 per enrollee (\$138 from NBCCEDP and \$395 from other sources); the cost of uncompensated care thus averaged \$523 per year per enrollee (approximately 50% of total cost). The net cost to the health system was nearly four dollars for each dollar of NBCCEDP revenue. The public health benefit of the NBCCEDP may extend beyond breast and cervical cancer but at a cost of increased uncompensated care borne by participating providers.

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Center for Health Services Research

Habib, Z. A., L. Tzogias, S. L. Havstad, K. Wells, G. Divine, D. E. Lanfear, J. Tang, R. Krajeta, M. Pladevall and L. K. Williams (2009). "Relationship between thiazolidinedione use and cardiovascular outcomes and all-cause mortality among patients with diabetes: a time-updated propensity analysis." Pharmacoepidemiology and Drug Safety **18**(6): 437-447. [Article Request Form](#)

[Williams, L. Keoki] Henry Ford Hlth Syst, Ctr Hlth Serv Res, Henry Ford Hosp, Detroit, MI 48202 USA. [Havstad, Suzanne L.; Wells, Karen; Divine, George; Krajeta, Richard; Williams, L. Keoki] Henry Ford Hosp, Dept Biostat & Res Epidemiol, Detroit, MI 48202 USA. [Habib, Zeina A.; Tzogias, Leonidas; Lanfear, David E.; Tang, Jeffrey; Williams, L. Keoki] Henry Ford Hosp, Dept Internal Med, Detroit, MI 48202 USA. Williams, LK, Henry Ford Hlth Syst, Ctr Hlth Serv Res, Henry Ford Hosp, 1 Ford Pl,3A CHSR, Detroit, MI 48202 USA. kwillia5@hfhs.org

Purpose To investigate the association of the thiazolidinediones (TZDs), rosiglitazone, and pioglitazone, together and individually on the risk of cardiovascular outcomes and all-cause mortality, using time-updated propensity score adjusted analysis. Methods We conducted a retrospective cohort study in a large vertically integrated health system in southeast Michigan. Cohort inclusion criteria included adult patients with diabetes treated with oral medications and followed longitudinally within the health system between 1 January 2000 and 1 December 2006. The primary outcome was fatal and non-fatal acute myocardial infarction (AMI). Secondary outcomes included hospitalizations for congestive heart failure (CHF), fatal, and non-fatal cerebrovascular accidents (CVA) and transient ischemic attacks (TIA), combined coronary heart disease (CHD) events, and all-cause mortality. Results 19 171 patients were included in this study. Use of TZDs (adjusted hazard ratio (aHR) with propensity adjustment (PA), 0.92; 95% confidence interval (CI) 0.73-1.17), rosiglitazone (aHR with PA, 1.06; 95%CI 0.66-1.70), and pioglitazone (aHR with PA, 0.91; 95%CI 0.69-1.21) was not associated with a higher risk of AMI. However, pioglitazone use was associated with a reduction in all-cause mortality (aHR with PA, 0.60; 95%CI 0.42-0.96). Compared with rosiglitazone, pioglitazone use was associated with a lower risk of all outcomes assessed, particularly CHF (p = 0.013) and combined CHD events (p = 0.048). Conclusions Our findings suggest that pioglitazone may have a more favorable risk profile when compared to rosiglitazone, arguing against a singular effect for TZDs on cardiovascular outcomes. Copyright (C) 2009 John Wiley & Sons, Ltd.

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Dermatology

Hamzavi, I., B. Mahmoud, E. Tierney, C. Hexsel, J. Pui and O. Ozog (2009). "Prospective Clinical and Histopathologic Study of Hidradenitis Suppurativa Treated with Laser." Lasers in Surgery and Medicine: 100-100. [Article Request Form](#)

[Hamzavi, Iltefat; Mahmoud, Bassel; Tierney, Emily; Hexsel, Camile; Pui, John; Ozog, Ozog] Henry Ford Hosp, Detroit, MI 48202 USA.

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Dermatology

Huggins, R. H., L. A. Leithauser, M. J. Eide, C. L. Hexsel, G. Jacobsen and H. W. Lim (2009). "Quality of life assessment and disease experience of patient members of a web-based hydroa vacciniforme support group." Photodermatology Photoimmunology & Photomedicine **25**(4): 209-215. [PDF Full-Text](#)

[Lim, Henry W.] Henry Ford Hosp, Dept Dermatol, Henry Ford Med Ctr, Detroit, MI 48202 USA. [Eide, Melody J.; Jacobsen, Gordon] Henry Ford Hosp, Dept Biostat & Res Epidemiol, Detroit, MI 48202 USA.

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Background/Purpose Hydroa vacciniforme (HV) is a rare photodermatosis that primarily affects children. It is characterized by photodistributed vesicles that heal with scarring. The purposes of this study are to perform the initial investigation into the effect of HV on quality of life (QoL) and gain insight into disease diagnosis and management. **Methods** Using the listserv from a web-based, international HV support group, either the Dermatology Life Quality Index (DLQI) or the Children's DLQI (CDLQI), and an HV-specific questionnaire were administered. **Results** Fifteen HV patients participated, nine (60%) males and six (40%) females. Median age at onset was 7 years, and 11/15 (73%) were younger than 18 years. The majority of patients were Caucasian (73%). Children cited life quality as being negatively impacted by an inability to play outdoors while adults noted QoL influences due to limitations on clothing choices. The mean CLDLQI and DLQI scores, 12.1 and 8.5, respectively, suggest a higher negative QoL impact than previously reported indices for generalized eczema, atopic dermatitis, and psoriasis. **Conclusion** When compared with other dermatoses, HV appears to have an equal or greater impact on patients' QoL. Dermatologists should be aware of the psychosociologic impact of this disease, especially on young HV patients.

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Dermatology

Marcus, D. V., B. H. Mahmoud and I. H. Hamzavi (2009). "Granuloma Annulare Treated With Rifampin, Ofloxacin, and Minocycline Combination Therapy." *Archives of Dermatology* **145**(7): 787-789. [PDF Full-Text](#)

[Marcus, Dione V.; Mahmoud, Bassel H.; Hamzavi, Iltefat H.] Henry Ford Hosp, Dept Dermatol, Detroit, MI 48202 USA.

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Background: Granuloma annulare (GA) is a benign, usually self-limiting, dermatosis, that typically presents as asymptomatic, flesh-colored or erythematous papules, frequently arranged in an annular or arciform pattern on the distal extremities. Although localized GA is most commonly observed, a generalized or disseminated form can occur. The etiology of GA is unknown; however, multiple inciting factors have been proposed. Histologically, GA is characterized by foci of degenerative collagen associated with palisading, sometimes infiltrating granulomatous inflammation. **Observations:** We report 6 cases with biopsy-proved GA, resistant to the standard modalities of treatment that resolved after 3 months with monthly rifampin (600 mg), ofloxacin (400 mg), and minocycline hydrochloride (100 mg) combination therapy. Rifampin, ofloxacin, and minocycline combination therapy has been successfully used to treat patients with paucibacillary leprosy. Given reports that prolonged antibiotic agents are a useful treatment for GA, rifampin (600 mg), ofloxacin (400 mg), and minocycline hydrochloride (100 mg) combination therapy was initiated in these patients. Complete clearance of the plaques was achieved 3 to 5 months after the initiation of treatment. Some patients experienced postinflammatory hyperpigmentation. **Conclusion:** Although our treatment was effective, further studies may be needed to confirm the success of this therapeutic option for patients with recalcitrant lesions of GA.

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Diagnostic Radiology

Arnold, R. T. and D. T. Myers (2009). "Visualization of renal angiomyolipoma on F-18 FDG PET/CT." *Clin Nucl Med* **34**(8): 539-40. [PDF Full-Text](#)

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Emergency Medicine

Birkhahn, R. H., E. Jauch, D. A. Kramer, R. M. Nowak, A. S. Raja, R. L. Summers, J. E. Weber, D. B. Diercks and S. I. R. C. on behalf of the (2009). "A Review of the Federal Guidelines That Inform and Influence Relationships Between Physicians and Industry." *Acad Emerg Med*. EPub Ahead of Print. [PDF Full-Text](#)

From the New York Methodist Hospital (RHB), Brooklyn, NY; Medical University of South Carolina (EJ), Charleston, SC; York Hospital (DAK), York, PA; Henry Ford Hospital (RMN), Detroit, MI; Brigham and Women's Hospital (ASR), Boston, MA; the University of Mississippi Medical Center (RLS), Jackson, MS; the University of Michigan (JEW), Ann Arbor, MI; Hurley Medical Center (JEW), Flint, MI; and the University of California, Davis Medical Center, Sacramento (DBD), CA.

Abstract The effective delivery and continued advancement of health care is critically dependent on the relationship between physicians and industry. The private sector accounts for 60% of the funding for clinical research and more than 50% of the funding sources for physician education. The nature of the physician-industry relationship and the role of the physician as a gatekeeper for health care make this association vulnerable to abuse if certain safeguards are not observed. This article will review the current federal guidelines that affect the physician-industry relationship and highlight several illustrative cases to show how the potential for abuse can subvert this relationship. The recommendations and "safe harbors" that have been designed to guide business relationships in health care are discussed. *ACADEMIC EMERGENCY MEDICINE* 2009; 16:1-6 (c) 2009 by the Society for Academic Emergency Medicine.

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Emergency Medicine

Manteuffel, J. (2009). "Use of antiemetics in children with acute gastroenteritis: Are they safe and effective?" *J Emerg Trauma Shock* 2(1): 3-5. PMC2700583. [Article Request Form](#)

Henry Ford Hospital, 2799 W. Grand Blvd, Detroit, MI 48201, USA.

The use of antiemetics is a controversial topic in treatment of pediatric gastroenteritis. Although not recommended by the American Academy of Pediatrics, antiemetics are commonly prescribed by physicians. A review of the literature shows side effects of promethazine, prochlorperazine, and metoclopramide are common and potentially dangerous. Ondansetron has recently been studied as an adjunct to oral rehydration therapy in treatment of acute gastroenteritis with mild to moderate dehydration. Although studies are limited, early research suggests the medication is safe when used in a single dose and can be effective to prevent vomiting, the need for intravenous fluids, and hospital admission.

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Eye Care Services

Kaufman, S. C. and J. S. Dhaliwal (2009). "Long Term Use of Topical Tacrolimus (FK506) in High-Risk Penetrating Keratoplasty Reply." *Cornea* 28(6): 716-716. [Article Request Form](#)

[Kaufman, Stephen C.] Univ Minnesota, Dept Ophthalmol, Minneapolis, MN 55455 USA. [Kaufman, Stephen C.; Dhaliwal, Jasmeet S.] Henry Ford Hlth Syst, Dept Ophthalmol, Troy, MI USA. Kaufman, SC, Univ Minnesota, Dept Ophthalmol, MMC 493,420 Delaware St SE,9th Floor, Minneapolis, MN 55455 USA. CorneaMD2000@Yahoo.com

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Eye Care Services

Rizzo, J. F., E. R. O'Malley and P. C. Hessburg (2009). "The Eye and The Chip 2008." *Journal of Neural Engineering* 6(3). [Article Request Form](#)

[Rizzo, Joseph F.] Harvard Univ, Sch Med, Boston, MA 02115 USA. [O'Malley, Edward R.] Henry Ford Eye Care Serv, Grosse Pointe Pk, MI USA. [Hessburg, Philip C.] Detroit Inst Ophthalmol, Grosse Pointe Pk, MI USA. Rizzo, JF, Harvard Univ, Sch Med, Boston, MA 02115 USA.

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Gastroenterology

Cheng, R., J. C. Barton, E. D. Morrison, P. D. Phatak, E. L. Krawitt, S. C. Gordon and K. V. Kowdley (2009). "Differences in Hepatic Phenotype Between Hemochromatosis Patients With HFE C282Y Homozygosity and Other HFE Genotypes." *Journal of Clinical Gastroenterology* 43(6): 569-573. [PDF Full-Text](#)

[Kowdley, Kris V.] Virginia Mason Med Ctr, Inst Digest Dis, Ctr Liver Dis, Seattle, WA 98101 USA. [Cheng, Raymond; Morrison, Elizabeth D.] Univ Washington, Dept Med, Seattle, WA 98195 USA. [Barton, James C.] So Iron Disorders Ctr, Birmingham, AL USA. [Phatak, Pradyumna D.] Univ Rochester, Rochester, NY USA. [Phatak, Pradyumna D.] Rochester Gen Hosp, Rochester, NY 14621 USA. [Krawitt, Edwards L.] Univ Vermont, Burlington, VT USA. [Gordon, Stuart C.] Henry Ford Hosp, Detroit, MI 48202 USA.
Kowdley, KV, Virginia Mason Med Ctr, Inst Digest Dis, Ctr Liver Dis, 1201 9th Ave, Seattle, WA 98101 USA.
kris.kowdley@vmmc.org

Objective: There are limited data comparing hepatic phenotype among hemochromatosis patients with different HFE genotypes. The goal of this study was to compare hepatic histopathologic features and hepatic iron concentration (HIC) among patients With phenotypic hemochromatosis and different HFE genotypes. Methods: We Studied 182 US patients with phenotypic hemochromatosis. Degree of hepatic fibrosis, pattern of iron deposition, presence of steatosis or necroinflammation, and HIC were compared among different HFE genotypes. Results: C282Y/H63D compound heterozygotes and patients with HFE genotypes other than C282Y/C282Y were more likely to have stainable Kupffer cell iron (31.1% vs. 9.5%; $P = 0.02$), portal or lobular inflammation (28.9% vs. 15.6%; $P = 0.03$), and steatosis (33.3% vs. 10.2%; $P < 0.01$) on liver biopsy than C282Y homozygotes. Mean $\log(10)$ HIC ($P < 0.05$) and $\log(10)$ ferritin ($P < 0.05$) were higher among C282Y homozygotes than in patients with other HFE genotypes. In it logistic regression analysis using age, sex, HFE genotype, $\log(10)$ Ferritin, and $\log(10)$ HIC as independent variables, $\log(10)$ serum ferritin ($P = 0.0008$), male sex ($P = 0.0086$), and $\log(10)$ HIC ($P = 0.047$), but not HFE genotype ($P = 0.0554$) were independently associated with presence or absence of advanced hepatic fibrosis. Conclusions: C282Y/H63D Compound heterozygotes and other non-C282Y homozygotes which express the hepatic hemochromatosis phenotype frequently have evidence of steatosis or chronic hepatitis and lower body iron stores than C282Y homozygotes. These data suggest that presence of concomitant liver disease may explain expression of the hemochromatosis phenotype among non-C282Y homozygotes. Increased age, HIC, and ferritin are associated with advanced hepatic fibrosis, regardless of HFE genotype.

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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." Clin Transplant. Epub Ahead of Print. [PDF Full-Text](#)

Division of Gastroenterology, Henry Ford Health Systems, Detroit, Michigan.

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

Raoufi, M., C. Ma, A. Ormsby, H. Vakil, K. Brown, M. A. Huang, D. Moonka and M. Abouljoud (2009). "The Role of Post-Reperfusion Biopsy in the Era of Extended Criteria Donor." Liver Transplantation 15(7): S266-S267. [PDF Full-Text](#)

[Brown, K.; Huang, M. A.; Moonka, D.] Henry Ford Hosp, Div Gastroenterol, Detroit, MI 48202 USA. [Abouljoud, M.] Henry Ford Hosp, Transplant Inst, Detroit, MI 48202 USA. [Vakil, H.] Wayne State Univ, Detroit, MI USA.

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Hematology, Medical Oncology & Josephine Ford Cancer Center

Lambing, A. and E. Kachalsky (2009). "The new age of haemophilia." Haemophilia. EPub Ahead of Print. [PDF Full-Text](#)

Hemophilia & Thrombosis Treatment Center, Henry Ford Health System, Detroit, MI, USA.

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Hematology, Medical Oncology & Josephine Ford Cancer Center

Simmons, T. L., L. M. Nogle, J. Media, F. A. Valeriote, S. L. Mooberry and W. H. Gerwick (2009). "Desmethoxymajusculamide C, a Cyanobacterial Depsipeptide with Potent Cytotoxicity in Both Cyclic and Ring-Opened Forms." Journal of Natural Products **72**(6): 1011-1016. [Article Request Form](#)

[Simmons, T. Luke; Gerwick, William H.] Univ Calif San Diego, Scripps Inst Oceanog, Ctr Marine Biotechnol & Biomed, La Jolla, CA 92037 USA. [Nogle, Lisa M.] Oregon State Univ, Coll Pharm, Corvallis, OR 97331 USA. [Media, Joseph; Valeriote, Frederick A.] Henry Ford Hosp, Josephine Ford Canc Ctr, Detroit, MI 48202 USA. [Mooberry, Susan L.] SW Fdn Biomed Res, San Antonio, TX 78245 USA. [Gerwick, William H.] Univ Calif San Diego, Skaggs Sch Pharm & Pharmaceut Sci, La Jolla, CA 92037 USA. Gerwick, WH, Univ Calif San Diego, Scripps Inst Oceanog, Ctr Marine Biotechnol & Biomed, La Jolla, CA 92037 USA. wgerwick@ucsd.edu

Cytotoxicity-guided fractionation of the organic extract from a Fijian *Lynngbya majuscula* led to the discovery of desmethoxymajusculamide C (DMMC) as the active metabolite. Spectroscopic analysis including 1D and 2D NMR, MS/MS, and chemical degradation and derivatization protocols were used to assign the planar structure and stereoconfiguration of this new cyclic depsipeptide. DMMC demonstrated potent and selective anti-solid tumor activity with an IC₅₀ = 20 nM against the HCT-116 human colon carcinoma cell line via disruption of cellular microfilament networks. A linear form of DMMC was generated by base hydrolysis, and the amino acid sequence was confirmed by mass spectrometry. Linearized DMMC was also evaluated in the biological assays and found to maintain potent actin depolymerization characteristics while displaying solid tumor selectivity equivalent to DMMC in the disk diffusion assay. A clonogenic assay assessing cytotoxicity to HCT-116 cells as a function of exposure duration showed that greater than 24 h of constant drug treatment was required to yield significant cell killing. Therapeutic studies with HCT-116 bearing SCID mice demonstrated efficacy at the highest dose used (%T/C = 60% at 0.62 mg/kg daily for 5 days).

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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. EPub Ahead of Print. [PDF Full-Text](#)

Department of Hematology/Oncology, Henry Ford Hospital, Detroit, Michigan.

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. *J. Clin. Apheresis* 2009. (c) 2009 Wiley-Liss, Inc.

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Hypertension & Vascular Research

Caceres, P. S., G. R. Ares and P. A. Ortiz (2009). "cAMP stimulates apical exocytosis of the renal Na-K-2Cl co-transporter NKCC2 in the thick ascending limb: Role of protein kinase A (PKA)." J Biol Chem. Epub Ahead of Print. [PDF Full-Text](#)

Henry Ford Hospital / Wayne State University, United States;

The apical renal Na-K-2Cl co-transporter NKCC2 mediates NaCl absorption by the thick ascending limb of Henle's loop (TAL). cAMP stimulates NKCC2 by enhancing steady-state apical membrane levels of this protein, however the trafficking and signaling mechanisms by which this occurs have not been studied. Here we report that stimulation of endogenous cAMP with either Forskolin/IBMX or a V2 receptor agonist dDAVP increases steady-state surface NKCC2 and that the PKA inhibitor H-89 blocks this effect. Confocal imaging of apical surface NKCC2 in isolated perfused TALs confirmed a stimulatory effect of cAMP on apical trafficking that was blocked by PKA inhibition. Selective stimulation of PKA with the agonist N(6)-Bnz-cAMP (500 μ M) stimulated steady-state surface NKCC2 whereas the Epac-selective agonist 8-pCPT-2-O-cAMP (100 and 250 μ M) had no effect. To explore the trafficking mechanism by which cAMP increases apical NKCC2, we measured cumulative apical membrane exocytosis and NKCC2 exocytic insertion in TALs. By monitoring apical FM1-43 fluorescence we observed rapid stimulation of apical exocytosis (2 min) by Forskolin/IBMX. We also found constitutive exocytic insertion of NKCC2 in TALs over time, which was increased by 3-fold in the presence of Forskolin/IBMX. PKA inhibition blunted cAMP-stimulated exocytic insertion but did not affect the rate of constitutive exocytosis. We concluded that cAMP stimulates steady-state apical surface NKCC2 by stimulating exocytic insertion and that this process is highly dependent on PKA but not Epac.

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Hypertension & Vascular Research

Hong, N. J. and J. L. Garvin (2009). "Nitric oxide reduces flow-induced superoxide production via cGMP-dependent protein kinase in thick ascending limbs." Am J Physiol Renal Physiol **296**(5): F1061-6. PMC2681368. [PDF Full-Text](#)

Hypertension and Vascular Research Division, Henry Ford Hospital, Detroit, MI 48202, USA.

We have shown that increased luminal flow induces O₂(⁻) and nitric oxide (NO) production in thick ascending limbs (TALs). However, the interaction of flow-stimulated NO and O₂(⁻) in TALs is unclear. We hypothesized that NO inhibits flow-induced O₂(⁻) production in TALs via cGMP-dependent protein kinase (PKG). We measured flow-stimulated O₂(⁻) production in rat TALs using dihydroethidium in the absence and presence of L-arginine (0.3 mM), the substrate for NO synthase. The addition of L-arginine reduced flow-induced net O₂(⁻) production from 68 \pm 9 to 17 \pm 4 AU/s ($P < 0.002$). The addition of the NO synthase inhibitor N(G)-nitro-L-arginine methyl ester (L-NAME; 5 mM) in the presence of L-arginine stimulated production (L-arginine: 15 \pm 4 AU/s vs. L-arginine + L-NAME: 63 \pm 7 AU/s; $P < 0.002$). The guanylate cyclase inhibitor LY-83583 (10 μ M) also enhanced flow-induced net O₂(⁻) production in the presence of L-arginine (L-arginine: 7 \pm 4 AU/s vs. L-arginine + LY-83583: 53 \pm 7 AU/s; $P < 0.01$). In the presence of LY-83583, L-arginine only reduced flow-induced net O₂(⁻) by 36% (LY-83583: 80 \pm 7 AU/s vs. LY-83583 + L-arginine: 51 \pm 3 AU/s; $P < 0.006$). The cGMP analog dibutyl (db)-cGMP reduced flow-induced net O₂(⁻) from 39 \pm 9 to 7 \pm 3 AU/s ($P < 0.03$). The PKG inhibitor KT-5823 (5 μ M) partially restored flow-induced net O₂(⁻) in the presence of L-arginine (L-arginine: 4 \pm 4 AU/s vs. L-arginine + KT-5823: 32 \pm 9 AU/s; $P < 0.03$) and db-cGMP (db-cGMP: 9 \pm 7 AU/s vs. db-cGMP + KT-5823: 54 \pm 5 AU/s; $P < 0.01$). Phosphodiesterase II inhibition had no effect on arginine-inhibited O₂(⁻) production. We conclude that 1) NO reduces flow-stimulated O₂(⁻) production, 2) this occurs primarily via the cGMP/PKG pathway, and 3) O₂(⁻) scavenging by NO plays a minor role.

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Hypertension & Vascular Research

Li, X. C., Y. Shao and J. L. Zhuo (2009). "AT(1a) receptor knockout in mice impairs urine concentration by reducing basal vasopressin levels and its receptor signaling proteins in the inner medulla." Kidney International **76**(2): 169-177. [PDF Full-Text](#)

[Li, Xiao C.; Shao, Yuan; Zhuo, Jia L.] Henry Ford Hosp, Div Hypertens & Vasc Res, Dept Internal Med, Lab Receptor & Signal Transduct, Detroit, MI 48202 USA. [Zhuo, Jia L.] Wayne State Univ, Sch Med, Dept Physiol, Detroit, MI 48201 USA.

Zhuo, JL, Henry Ford Hosp, Div Hypertens & Vasc Res, Dept Internal Med, Lab Receptor & Signal Transduct, 2799 W Grand Blvd, Detroit, MI 48202 USA. jzhuo1@hfhs.org

Angiotensin II plays an important role in the regulation of blood pressure, body salt and fluid balance, and urine concentration. Mice with deletion of the AT(1a) receptor develop polyuria and urine concentration defects. We studied the mechanisms of these urine concentration defects by treating wild-type and AT(1a)-knockout mice with arginine vasopressin (AVP) for 2 weeks, controlling their water intake, or giving them an osmotic diuretic (sucrose) in order to determine whether central or nephrogenic mechanisms were involved. Under basal conditions, AT(1a)-knockout mice were hypotensive, had lower plasma AVP, and excreted more urine with a markedly reduced osmolality compared with wild-type mice. However, basal glomerular filtration rates were similar in both strains of mice. We isolated total lysate and membrane proteins from the inner medulla of wild-type and mutant mouse kidneys, and found that the amounts of aquaporin 2 (AQP2), adenylyl cyclases III and V/VI, and phosphorylated MAP kinases ERK 1/2 proteins were all reduced in the inner medulla of the knockout mice. Infusion of AVP raised plasma levels and blood pressure proportionally in both strains, but polyuria persisted and urine osmolality remained significantly lower in the knockout mice. Although AVP increased urine osmolality slightly in water-deprived knockout mice, this was well below the basal osmolality of wild-type mice. The diuretic response to the hyperosmotic sucrose was also impaired in the knockout mice. Neither AVP nor water rationing restored the levels of the inner medullary signaling proteins and membrane AQP2 proteins in the knockout mice. We suggest that AT(1a) receptor deletion causes polyuria and urine concentration defects by decreasing basal AVP release and impairing AVP-induced receptor signaling in the inner medulla. *Kidney International* (2009) 76, 169-177; doi: 10.1038/ki.2009.134; published online 22 April 2009

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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." *Am J Physiol Renal Physiol*. EPub Ahead of Print. [PDF Full-Text](#)

Henry Ford Hospital.

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 a) NO in TALs using the NO-sensitive dye DAF-2 DA and b) Akt activity by fluorescence resonance energy transfer (FRET) and phosphorylation of Akt isoforms. ATP (100 microM) stimulated NO in wild-type mice (26+/-4 arbitrary units, AU), but not in NOS3 -/- mice (2+/-2 AU; p<0.04). In the presence of the NOS1 and NOS2 selective inhibitors 7-NI and 1400W, ATP stimulated NO by 30+/-2 AU and 33+/-3 AU, respectively (N.S. 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. Key words: ATP, P2 receptors, NKCC2, kidney.

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Infectious Diseases

Moore, C. L., A. Hingwe, S. M. Donabedian, M. B. Perri, S. L. Davis, N. Z. Haque, K. Reyes, D. Vager and M. J. Zervos (2009). "Comparative evaluation of epidemiology and outcomes of methicillin-resistant *Staphylococcus aureus* (MRSA) USA300 infections causing community- and healthcare-associated infections." *International Journal of Antimicrobial Agents* **34**(2): 148-155. [Article Request Form](#)

[Moore, Carol L.] Henry Ford Hlth Syst, Div Infect Dis, CFP3, Detroit, MI 48202 USA. [Davis, Susan L.] Eugene Applebaum Coll Pharm & Hlth Sci, Detroit, MI USA. [Zervos, Marcus J.] Wayne State Univ, Sch Med, Detroit, MI USA.

Moore, CL, Henry Ford Hlth Syst, Div Infect Dis, CFP3, 2799 W Grand Blvd, Detroit, MI 48202 USA. cmoore2@hfhs.org

Methicillin-resistant Staphylococcus aureus (MRSA) USA300 clone is commonly found in the community and is being increasingly reported in the healthcare setting. A retrospective analysis was conducted to compare the epidemiology and outcomes between community-associated (CA) and healthcare-associated (HA) USA300 MRSA infections. The study enrolled 160 subjects with USA300 MRSA infections (47.5% CA-MRSA and 52.5% HA-MRSA). Failure in the HA group was higher (38.1%) compared with the CA group (23.7%) (P = 0.05). Predictors of failure included male gender, age, presence of any co-morbidity, coronary artery disease, chronic kidney disease, history of MRSA, previous admission, fluoroquinolone exposure, HA infection and osteomyelitis (P <= 0.05). Independent predictors of failure were osteomyelitis, history of MRSA, male gender and pneumonia. Recurrent disease was found in 32.6% of cases. Overall, USA300 MRSA most commonly causes infection of the skin and skin structure, however, 20% of subjects can experience more invasive disease with infection of the bloodstream, lung or bone. Failure rates are higher in subjects with healthcare risk factors or if the infection was acquired in the hospital, with these subjects experiencing more invasive infections such as bacteraemia, pneumonia or osteomyelitis. (C) 2009 Elsevier B. V. and the International Society of Chemotherapy. All rights reserved.

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Internal Medicine

Kanjanauthai, S. and T. Kanluen (2009). "Painless acute aortic dissection presenting as left lower extremity weakness and numbness." Heart Lung Circ **18**(2): 133-5. [Article Request Form](#)

Department of Internal Medicine, Henry Ford Hospital, Detroit, MI 48202, United States. somsupha@hotmail.com

Acute aortic dissection usually presents with a sudden, painful, tearing sensation in the chest or back. However, acute aortic dissection may also present atypically without pain and with solely neurological symptoms. We describe a case of painless acute aortic dissection which presented as acute left lower extremity weakness and numbness. These neurological symptoms are due to vascular occlusion causing peripheral ischaemic neuropathy. It is imperative to consider acute aortic dissection in the differential diagnosis of acute neurological syndromes.

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Internal Medicine

Mahmoud, B., D. Srivastava, D. Ozog, D. Kouba and E. Tierney (2009). "THE TREATMENT OF SURGICAL SCARS WITH FRACTIONAL PHOTOTHERMOLYSIS vs PULSE DYE LASER, A RANDOMIZED CONTROL TRIAL." Lasers in Surgery and Medicine: 86-86. [Article Request Form](#)

Henry Ford Hlth Syst, Detroit, MI USA. Laser & Skin Surg Ctr Indiana, Carmel, IN USA.

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Internal Medicine

Sandhu, A., T. J. Yates and P. Kuriakose (2008). "Pulmonary artery sarcoma mimicking a pulmonary embolism." Indian J Cancer **45**(1): 27-9. [PDF Full-Text](#)

Departments of Internal Medicine, Henry Ford Hospital, 2799 West Grand Blvd, Detroit, MI 48202, USA.

Sarcomas involving the lung are a rare occurrence, often a result of metastatic disease from primary malignancies involving the skin, liver, breast or heart. Primary pulmonary artery sarcomas are rarer still, with limited cases reported world-wide and consequently data regarding treatment modalities are sparse and largely experimental. These tumors are often mistaken for a pulmonary embolism and seemingly supported by radiological findings. Patients will often present without symptom resolution despite therapeutic anticoagulation. The following case illustrates how a soft tissue sarcoma of the pulmonary artery can mimic a pulmonary embolism, thus, resulting in both a diagnostic and therapeutic dilemma. A positron emission tomography scan was an invaluable tool in this case, showing increased radiotracer uptake and placing neoplasm at the top of the differential diagnosis. This ultimately led to a biopsy that was vimentin positive, cytokeratin negative and CD117 negative, thus consistent with soft tissue sarcoma.

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Internal Medicine

Yan, B., A. M. Noone, C. Yee, M. Banerjee, K. Schwartz and M. S. Simon (2009). "Racial differences in colorectal cancer survival in the Detroit Metropolitan area." Cancer **115**(16): 3791-3800. [PDF Full-Text](#)

Department of Internal Medicine, Henry Ford Hospital and Medical Center, Detroit, Michigan.

BACKGROUND:: Colorectal carcinoma is the second most common cause of cancer death with African Americans having lower survival compared with White Americans. The purpose of this study was to investigate the effect of demographics, clinical factors, and socioeconomic status (SES) on racial disparities in colorectal cancer survival in the Detroit Metropolitan Area. **METHODS::** The study population included 9078 individuals with primary invasive colorectal cancer identified between 1988 and 1992 through the Surveillance, Epidemiology, and End Results (SEER) program. Demographics, clinical information, and survival were obtained through SEER. SES was categorized using occupation, educational level, and poverty status at the census tract level. Kaplan-Meier survival curves and Cox proportional hazards regression were used to compare overall survival by race. **RESULTS::** African Americans were more likely to be diagnosed with stage IV disease ($P < .001$), and to reside within poor census tracts ($P < .001$) compared with White Americans. Unadjusted analysis showed that African Americans had a significantly higher risk of death compared with their White American counterparts (hazards ratio [HR], 1.13; 95% confidence interval [CI], 1.07-1.20). After adjusting for age, marital status, sex, SES group, TNM stage, and treatment, race was no longer significantly associated with overall survival (HR, 1.00; 95% CI, 0.92-1.09). Similar results were seen with colorectal cancer-specific survival. **CONCLUSIONS::** Racial disparities in colorectal cancer survival dissipate after adjusting for other demographic and clinical factors. These results can potentially affect medical guidelines regarding screening and treatment, and possibly influence public health policies that can have a positive impact on equalizing racial differences in access to care. *Cancer* 2009. (c) 2009 American Cancer Society.

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Nephrology

Boudville, N. C., O. Djurdjev, I. C. Macdougall, A. L. M. de Francisco, G. Deray, A. Besarab, P. E. Stevens, R. G. Walker, P. Urena, P. Inigo, R. Minutolo, Y. S. Haviv, K. Yeates, M. L. Aguera, J. M. MacRae and A. Levin (2009). "Hemoglobin Variability in Nondialysis Chronic Kidney Disease: Examining the Association with Mortality." Clinical Journal of the American Society of Nephrology **4**(7): 1176-1182. [Article Request Form](#)

[Boudville, Neil C.] Univ Western Australia, Sch Med & Pharmacol, Nedlands, WA 6009, Australia. [Boudville, Neil C.] Sir Charles Gairdner Hosp, Dept Renal Med, Perth, WA 6000, Australia. [Djurdjev, Ognjenka; Levin, Adeera] Univ British Columbia, St Pauls Hosp, Div Nephrol, Dept Med, Vancouver, BC V5Z 1M9, Canada. [Macdougall, Iain C.; Agueera, Marisa L.] Kings Coll London Hosp, Dept Renal Med, London, England. [de Francisco, Angel L. M.] Hosp Univ Valdecilla, Serv Nefrol, Santander, Spain. [Deray, Gilbert] Hosp Pitie Salpetriere, Dept Nephrol, Paris, France. [Besarab, Anatole] Henry Ford Hlth Syst, Div Nephrol & Hypertens, Dept Med, Detroit, MI USA. [Stevens, Paul E.] Kent & Canterbury Hosp, Dept Renal Med, Canterbury, Kent, England. [Walker, Rowan G.] Royal Melbourne Hosp, Dept Nephrol, Melbourne, Vic 3050, Australia. [Urena, Pablo] Clin Landy, Serv Nephrol Dialyse, St Ouen, France. [Inigo, Pablo] Hosp Clin Univ Lozano Blesa, Serv Nefrol, Zaragoza, Spain. [Minutolo, Roberto] Univ Naples 2, Dept Nephrol, Naples, Italy. [Haviv, Yosef S.] Hadassah Hebrew Univ, Med Ctr, Div Nephrol, Jerusalem, Israel. [Yeates, Karen] Queens Univ, Dept Med, Kingston, ON K7L 3N6, Canada. [Aguera, Marisa L.] Hosp Univ Reina Sofia, Serv Nefrol, Cordoba, Spain. [MacRae, Jennifer M.] Foothills Med Ctr, Div Nephrol, Calgary, AB, Canada.

Boudville, NC, Sir Charles Gairdner Hosp, Sch Med & Pharmacol, M503,4th Floor G Block, Verdun St, Nedlands, WA 6009, Australia. neil.boudville@uwa.edu.au

Background and objectives: Anemia and hemoglobin (Hb) variability are associated with mortality in hemodialysis patients who are on erythropoiesis-stimulating agents (ESA). Our aim was to describe the degree of Hb variability present in nondialysis patients with chronic kidney disease (CKD), including those who were not receiving ESA, and to investigate the association between Hb variability and mortality. **Design, setting, participants, & measurements:** Hb variability was determined using 6 mo of "baseline" data between January 1, 2003, and October 31, 2005. A variety of definitions for Hb variability were examined to ensure consistency and robustness. **Results:** A total of 6165 patients from 22 centers in seven countries were followed for a mean of 34.0 +/- 15.8 mo; 49% were prescribed an ESA. There was increased Hb variability with ESA use; the residual SD of Hb was 4.9 +/- 4.4 g/L in patients who were not receiving an ESA, compared with 6.8 +/- 4.8 g/L. Hb variability was associated with a small but significantly increased risk for death per g/L residual SD, irrespective of ESA use. Multivariate linear regression model explained only 11% of the total variance of Hb variability. **Conclusions:** Hb variability is

increased in patients who have CKD and are receiving ESA and is associated with an increased risk for death (even in those who are not receiving ESAs). This analysis cannot determine whether Hb variability causally affects mortality. Thus, the concept of targeting Hb variability with specific agents needs to be examined within the context of factors that affect both Hb variability and mortality. Clin J Am Soc Nephrol 4: 1176-1182, 2009. doi: 10.2215/CJN.04920908

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Neurology

Camp, D. M., D. A. Loeffler, D. M. Farrah, J. N. Borneman and P. A. LeWitt (2009). "Cellular immune response to intrastrially implanted allogeneic bone marrow stromal cells in a rat model of Parkinson's disease." Journal of Neuroinflammation **6**. [PDF Full-Text](#)

[Camp, Dianne M.; Loeffler, David A.; Farrah, Diane M.] William Beaumont Hosp, Res Inst, Div Neurol, Royal Oak, MI 48073 USA. [Borneman, Jade N.] Cognate Bioserv, Baltimore, MD USA. [LeWitt, Peter A.] Henry Ford Hosp, Dept Neurol, Detroit, MI 48034 USA.

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Background: Marrow stromal cells (MSC), the non-hematopoietic precursor cells in bone marrow, are being investigated for therapeutic potential in CNS disorders. Although in vitro studies have suggested that MSC may be immunologically inert, their immunogenicity following transplantation into allogeneic recipients is unclear. The primary objective of this study was to investigate the cellular immune response to MSC injected into the striatum of allogeneic recipients (6-hydroxydopamine [6-OHDA]-hemilesioned rats, an animal model of Parkinson's disease [PD]), and the secondary objective was to determine the ability of these cells to prevent nigrostriatal dopamine depletion and associated motor deficits in these animals. Methods: 5-Bromo-2-deoxyuridine (BrdU) - labeled MSC from two allogeneic sources (Wistar and ACI rats) were implanted into the striatum of adult Wistar rats at the same time as 6-OHDA was administered into the substantia nigra. Behavioral tests were administered one to two weeks before and 16-20 days after 6-OHDA lesioning and MSC transplantation. Immunocytochemical staining for T helper and T cytotoxic lymphocytes, microglia/macrophages, and major histocompatibility class I and II antigens was performed on post-transplantation days 22-24. MSC were detected with an anti-BrdU antibody. Results: Tissue injury due to the transplantation procedure produced a localized cellular immune response. Unexpectedly, both sources of allogeneic MSC generated robust cellular immune responses in the host striatum; the extent of this response was similar in the two allograft systems. Despite these immune responses, BrdU(+) cells (presumptive MSC) remained in the striatum of all animals that received MSC. The numbers of remaining MSC tended to be increased ($p = 0.055$) in rats receiving Wistar MSC versus those receiving ACI MSC. MSC administration did not prevent behavioral deficits or dopamine depletion in the 6-OHDA-lesioned animals. Conclusion: MSC, when implanted into the striatum of allogeneic animals, provoke a marked immune response which is not sufficient to clear these cells by 22-24 days post-transplantation. In the experimental paradigm in this study, MSC did not prevent nigrostriatal dopamine depletion and its associated behavioral deficits. Additional studies are indicated to clarify the effects of this immune response on MSC survival and function before initiating trials with these cells in patients with PD or other neurodegenerative disorders.

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Neurology

Cerghet, M., R. P. Skoff, M. Swamydas and D. Bessert (2009). "Sexual dimorphism in the white matter of rodents." J Neurol Sci. Epub Ahead of Print. [PDF Full-Text](#)

Henry Ford Health System, United States.

Sexual dimorphism of astrocytes and neurons is well documented in many brain and spinal cord structures. Sexual dimorphism of oligodendrocytes (Olg) and myelin has received less attention. We recently showed that density of Olg in corpus callosum, fornix, and spinal cord of wild-type male rodents is more densely packed than in females; myelin proteins and myelin gene expression are likewise greater in males than in female rodents. However, glial cell proliferation and cell death were two times greater in female corpus callosum. Endogenous sex hormones, specifically lack of androgens, produce an Olg female phenotype in castrated male mouse. In vitro studies using Olg culture also showed differences between males and females Olg survival and signaling pathways in response to sexual hormones. Sexual dimorphism of white matter tracts and glia in rodents indicates the necessity for controlling gender in the experimental studies of neurodegenerative disorders. Most importantly, our studies

suggest that hormones may contribute to sexual dimorphism observed in certain human diseases including multiple sclerosis.

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Neurology

Chen, J. L., X. Cui, A. Zacharek, C. Roberts and M. Chopp (2009). "eNOS Mediates TO90317 Treatment-Induced Angiogenesis and Functional Outcome After Stroke in Mice." *Stroke* **40**(7): 2532-2538. [PDF Full-Text](#)

[Chen, Jieli; Cui, Xu; Zacharek, Alex; Roberts, Cynthia; Chopp, Michael] Henry Ford Hosp, Dept Neurol, Detroit, MI 48202 USA. [Chopp, Michael] Oakland Univ, Dept Phys, Rochester, MI USA.

Chen, JL, Henry Ford Hosp, Dept Neurol, E&R Bldg, Room 3091, 2799 W Grand Blvd, Detroit, MI 48202 USA. jieli@neuro.hfh.edu

Background and Purpose-TO901317, a synthetic liver X receptor agonist, elevates high-density lipoprotein cholesterol (HDL-C) in mice. We tested the hypothesis that TO901317 treatment of stroke promotes angiogenesis and vascular maturation and improves functional outcome after stroke by increasing endothelial nitric oxide synthase (eNOS) phosphorylation. **Methods**-C57BL/6J mice were subjected to middle cerebral artery occlusion and were treated with or without TO901317 (30 mg/kg) starting 24 hours after middle cerebral artery occlusion and daily for 14 days. **Results**-TO901317 significantly increased serum HDL-C level, promoted angiogenesis and vascular stabilization in the ischemic brain, and improved functional outcome after stroke. The increased HDL-C level significantly correlated with functional recovery after stroke. TO901317 also increased eNOS phosphorylation in the ischemic brain. Mechanisms underlying the TO901317-induced angiogenesis were investigated using eNOS knockout (eNOS^{-/-}) mice. TO901317 treatment of eNOS^{-/-} mice significantly increased HDL-C level but failed to increase angiogenesis and functional outcome after stroke. In vitro studies demonstrated that TO901317 and HDL-C significantly increased capillary tube formation and promoted eNOS phosphorylation activity in cultured mouse brain endothelial cells compared with nontreatment controls. However, TO901317 and high-density lipoprotein treatment-induced capillary tube formation were absent in eNOS-deficient mouse brain endothelial cell.

Conclusions-These data indicate that TO901317 treatment increases serum HDL-C level, which promotes angiogenesis through eNOS and leads to improvement of functional outcome after stroke. (*Stroke*. 2009; 40: 2532-2538.)

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Neurology

Cui, X., M. Chopp, A. Zacharek, C. Roberts, M. Lu, S. Savant-Bhonsale and J. Chen (2009). "Chemokine, vascular and therapeutic effects of combination Simvastatin and BMSC treatment of stroke." *Neurobiol Dis*. Epub Ahead of Print. [Article Request Form](#)

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We investigated the additive therapeutic effect of the combination treatment of stroke with sub-therapeutic doses of Simvastatin, a HMG-CoA reductase inhibitor, and bone marrow stromal cells (BMSCs). Rats were administered Simvastatin (0.5 mg/kg), BMSCs (1x10⁶) or combination of Simvastatin and BMSCs starting at 24 h after stroke. Combination treatment significantly improved neurological outcome, enhanced angiogenesis and arteriogenesis, and increased the number of engrafted-BMSCs in the ischemic brain. The number of engrafted-BMSCs and arteriogenesis was significantly correlated with functional outcome. Simvastatin significantly increased stromal cell-derived factor-1 (SDF1) expression in the ischemic brain and chemokine (CXC motif) receptor-4 (CXCR4) in BMSCs, and increased BMSC migration to RBMECs and astrocytes. Combination treatment of stroke upregulates the SDF1/CXCR4 axis and enhances BMSC migration into the ischemic brain, amplifies arteriogenesis and angiogenesis, and improves functional outcome after stroke.

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Neurology

Liu, Z. W., R. L. Zhang, Y. Li, Y. S. Cui and M. Chopp (2009). "Remodeling of the Corticospinal Innervation and Spontaneous Behavioral Recovery After Ischemic Stroke in Adult Mice." *Stroke* **40**(7): 2546-2551. [PDF Full-Text](#)

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Background and Purpose-To elucidate how the motor pathways rewire the denervated tissue after stroke, we investigated remodeling of the corticospinal tract (CST) in transgenic mice with yellow fluorescent protein CST labeling in conjunction with transsynaptic pseudorabies virus retrograde tracing. **Methods-**Adult male CST-yellow fluorescent protein mice were subjected to permanent right middle cerebral artery occlusion (n = 8/group). Foot-fault test was performed to monitor functional deficit and recovery. Pseudorabies virus tracer was injected into the left forelimb muscles at 1 or 4 weeks after middle cerebral artery occlusion (4 days before euthanasia), respectively. A third group of CST-yellow fluorescent protein mice without middle cerebral artery occlusion was used for normal control (n = 6). The yellow fluorescent protein labeling of CST in the cervical cord and pseudorabies virus labeling of pyramidal neurons in the bilateral cortices were measured on vibratome sections using a confocal imaging system. **Results-**Compared with normal animals, axonal density in the stroke-affected side of the cervical cord was significantly decreased at 11 days (P < 0.001) and significantly increased at 32 days after stroke compared with the Day 11 values (P < 0.05). Pseudorabies virus labeling was significantly decreased in the ischemic hemisphere 11 days after middle cerebral artery occlusion (P < 0.001). In contrast, a significant increase was observed in pseudorabies virus labeling of bilateral cortices 32 days after stroke compared with 11 days (P < 0.05). The CST axonal density in the denervated spinal cord and pyramidal neuron labeling in the bilateral cortices were significantly correlated with behavioral recovery (P < 0.05). **Conclusions-**Spontaneous functional recovery after stroke may, at least in part, be attributed to neuronal remodeling in the corticospinal system. (Stroke. 2009; 40: 2546-2551.)

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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. Epub Ahead of Print. [Article Request Form](#)

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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. **CONCLUSION:** 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

Zhang, R. L., M. Chopp, S. R. Gregg, Y. Toh, C. Roberts, Y. LeTourneau, B. Buller, L. F. Jia, S. P. N. Davarani and Z. G. Zhang (2009). "Patterns and dynamics of subventricular zone neuroblast migration in the ischemic striatum of the adult mouse." Journal of Cerebral Blood Flow and Metabolism 29(7): 1240-1250. [Article Request Form](#)

[Zhang, Rui L.; Chopp, Michael; Gregg, Sara R.; Toh, Yier; Roberts, Cindi; LeTourneau, Yvonne; Buller, Benjamin; Jia, Longfei; Davarani, Siamak P. Nejad; Zhang, Zheng G.] Henry Ford Hlth Sci Ctr, Dept Neurol, Detroit, MI 48202 USA. [Chopp, Michael; Buller, Benjamin] Oakland Univ, Dept Phys, Rochester, MI USA.
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The migratory behavior of neuroblasts after a stroke is poorly understood. Using time-lapse microscopy, we imaged migration of neuroblasts and cerebral vessels in living brain slices of adult doublecortin (DCX, a marker of neuroblasts) enhanced green fluorescent protein (eGFP) transgenic mice that were subjected to 7 days of stroke. Our results show that neuroblasts originating in the subventricular zone (SVZ) of adult mouse brain laterally migrated in chains or individually to reach the ischemic striatum. The chains were initially formed at the border between the SVZ and the striatum by neuroblasts in the SVZ and then extended to the striatum. The average speed of DCX-eGFP-expressing cells within chains was 28.67 +/- 1.04 μ m/h, which was significantly faster ($P < 0.01$) than the speed of the cells in the SVZ (17.98 +/- 0.57 μ m/h). Within the ischemic striatum, individual neuroblasts actively extended or retracted their processes, suggestive of probing the immediate microenvironment. The neuroblasts close to cerebral blood vessels exhibited multiple processes. Our data suggest that neuroblasts actively interact with the microenvironment to reach the ischemic striatum by multiple migratory routes. *Journal of Cerebral Blood Flow & Metabolism* (2009) 29, 1240-1250; doi: 10.1038/jcbfm.2009.55; published online 13 May 2009

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Neurology

Zhang, X. P., X. G. Zheng, F. Jiang, Z. G. Zhang, M. Katakowski and M. Chopp (2009). "Dual-color fluorescence imaging in a nude mouse orthotopic glioma model." *Journal of Neuroscience Methods* **181**(2): 178-185. [Article Request Form](#)

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We sought to establish a new orthotopic glioma model of nude mice by transfer of DsRed2, a red fluorescent protein gene, to malignant glioma cells and to perfuse the tissue with fluorescein isothiocyanate (FITC) dextran in vivo, which would permit the concurrent detection of brain tumor invasion and angiogenesis in vivo by fluorescence microscopy. 9L or U87 malignant glioma cells with DsRed2 expression were intracerebrally injected into the nude mice. FITC-dextran was administered intravenously to the mice bearing DsRed2-9L or DsRed2-U87 cells immediately before they were sacrificed at 10 days or 15 days after the implantation, respectively. Coronal vibratome sections were examined using 2D and 3D fluorescence microscopy and the results were compared with those examined by routine hematoxylin and eosin (H & E) staining. Angiogenesis induced by glioma was confirmed by two-dimensional and three-dimensional imaging analysis. DsRed2 fluorescence clearly demarcated the primary tumor margins and readily allowed for the visualization of local invasion at the single-cell level in the brain adjacent to tumor. We found that a few tumor cells migrated from the tumor mass along the aberrant microvasculature, but did not extend out of the angiogenic areas. However, locally invasive foci were very difficult to detect by H & E staining. We demonstrated, for the first time, that abnormal vascular structure and glioma cells can be visualized concurrently by fluorescence microscopy. This method is superior to H & E staining for the detection and study of physiologically relevant patterns of brain tumor invasion and angiogenesis in vivo. (C) 2009 Elsevier B.V. All rights reserved.

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Neurosurgery

Chang, V., P. Hartzfeld, M. Langlois, A. Mahmood and D. Seyfried (2009). "Outcomes of cranial repair after craniectomy." *J Neurosurg*. Epub Ahead of Print. [PDF Full-Text](#)

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

Object Hemicraniectomy is a commonly practiced neurosurgical intervention with a wide range of indications and clinical data supporting its use. The extensive use of this procedure directly results in more cranioplasties to repair

skull defects. The complication rate for cranial repair after craniectomy seems to be higher than that of the typical elective craniotomy. This finding prompted the authors to review their experience with patients undergoing cranial repair. Methods The authors performed a retrospective review of 212 patients who underwent cranial repair over a 13-year period at their institution. A database tracking age, presenting diagnosis, side of surgery, length of time before cranial repair, bone graft material used, presence of a ventricular shunt, presence of a postoperative drain, and complications was created and analyzed. Results The overall complication rate was 16.4% (35 of 213 patients). Patients 0-39 years of age had the lowest complication rate of 8% ($p = 0.028$). For patients 40-59 years of age and older than 60, complication rates were 20 and 26%, respectively. Patients who originally presented with traumatic injuries had a lower rate of complications than those who did not (10 vs 20%; $p = 0.049$). Conversely, patients who presented with tumors had a higher complication rate than those without (38 vs 15%; $p = 0.027$). Patients who received autologous bone graft placement had a statistically significant lower risk of postoperative infection (4.6 vs 18.4%; $p = 0.002$). Patients who underwent cranioplasty with a 0-3 month interval between operations had a complication rate of 9%, 3-6 months 18.8%, and > 6 months 26%. Pairwise comparisons showed that the difference between the 0-3 month interval and the > 6 -month interval was significant ($p = 0.007$). The difference between the 0-3 month interval and the 4-6 month interval showed a trend ($p = 0.07$). No difference was detected between the 4-6 month interval and > 6 -month interval ($p = 0.35$). Conclusions The overall rate of complications related to cranioplasty after craniectomy is not negligible, and certain factors may be associated with increased risk. Therefore, when evaluating the need to perform a large decompressive craniectomy, the surgeon should also be aware that the patient is not only subject to the risks of the initial operation, but also the risks of subsequent cranioplasty.

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Neurosurgery

Li, B., A. Mahmood, D. Lu, H. Wu, Y. Xiong, C. Qu and M. Chopp (2009). "Simvastatin attenuates microglial cells and astrocyte activation and decreases interleukin-1beta level after traumatic brain injury." Neurosurgery **65**(1): 179-85; discussion 185-6. [PDF Full-Text](#)

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

OBJECTIVE: Our previous studies demonstrated that simvastatin promotes neurological functional recovery after traumatic brain injury (TBI) in rat; however, the underlying mechanisms remain poorly understood. The purpose of this study was to investigate the anti-inflammatory effect of simvastatin by measuring the level of cytokines and activation of glial cells. METHODS: Controlled cortical impact injury was performed in adult male Wistar rats. The rats were randomly divided into 3 groups: sham, saline control group, and simvastatin treatment group. Simvastatin was administered orally starting at day 1 after TBI until animals were killed at days 1, 3, 7, 14, and 35 after treatment. Functional outcome was measured using modified neurological severity scores. Enzyme-linked immunosorbent assay and immunohistochemical staining were used to measure the expression of interleukin (IL)-1beta, IL-6, and tumor necrosis factor-alpha and to identify activated microglial cells and astrocytes. RESULTS: At days 1 and 3 after simvastatin or saline treatment, cytokine levels in the lesion boundary zone were significantly higher in the simvastatin- and saline-treated rats compared with the sham group, peaking at day 3. Simvastatin only reduced the level of IL-1beta but not IL-6 and tumor necrosis factor-alpha, compared with the saline group. Also, simvastatin significantly reduced the number of activated microglial cells and astrocytes compared with the saline control animals. There was also a trend toward improvement of modified neurological severity score, reaching statistical significance ($P = 0.003$) toward the end of the trial. CONCLUSION: Our data demonstrate that TBI causes inflammatory reaction, including increased levels of IL-1beta, IL-6, and tumor necrosis factor-alpha, as well as activated microglial cells. Simvastatin selectively reduces IL-1beta expression and inhibits the activation of microglial cells and astrocytes after TBI, which might be one of the mechanisms underlying the therapeutic benefits of simvastatin treatment of TBI.

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Neurosurgery

Lomonaco, S. L., S. Finniss, C. L. Xiang, A. DeCarvalho, F. Umansky, S. N. Kalkanis, T. Mikkelsen and C. Brodie (2009). "The induction of autophagy by gamma-radiation contributes to the radioresistance of glioma stem cells." International Journal of Cancer **125**(3): 717-722.

[PDF Full-Text](#)

[Lomonaco, Stephanie L.; Finniss, Susan; Xiang, Cunli; DeCarvalho, Ana; Umansky, Felix; Kalkanis, Steven N.; Mikkelsen, Tom; Brodie, Chaya] Henry Ford Hosp, Dept Neurosurg, Hermelin Brain Tumor Ctr, William & Karen

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Malignant gliomas are characterized by a short median survival which is largely impacted by the resistance of these tumors to chemo- and radiotherapy. Recent studies suggest that a small subpopulation of cancer stem cells, which are highly resistant to gamma-radiation, has the capacity to repopulate the tumors and contribute to their malignant progression. gamma-radiation activates the process of autophagy and inhibition of this process increases the radiosensitivity of glioma cells; however, the role of autophagy in the resistance of glioma stem cells (GSCs) to radiation has not been yet reported. In this study we examined the induction of autophagy by gamma-radiation in CD133+ GSCs. Irradiation of CD133+ cells induced autophagy within 24-48 hr and slightly decreased the viability of the cells. gamma-radiation induced a larger degree of autophagy in the CD133+ cells as compared with CD133- cells and the CD133+ cells expressed higher levels of the autophagy-related proteins LC3, ATG5 and ATG12. The autophagy inhibitor bafilomycin A1 and silencing of ATG5 and beclin1 sensitized the CD133+ cells to I-radiation and significantly decreased the viability of the irradiated cells and their ability to form neurospheres. Collectively, these results indicate that the induction of autophagy contributes to the radioresistance of these cells and autophagy inhibitors may be employed to increase the sensitivity of CD133+ GSCs to gamma-radiation. (C) 2009 UICC

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Neurosurgery

Mahmood, A., A. Goussev, H. Kazmi, C. Qu, D. Lu and M. Chopp (2009). "Long-term benefits after treatment of traumatic brain injury with simvastatin in rats." *Neurosurgery* **65**(1): 187-91; discussion 191-2. [PDF Full-Text](#)

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OBJECTIVE: This study was designed to investigate the long-term effects of simvastatin treatment after traumatic brain injury (TBI) in rats. METHODS: Adult female Wistar rats (n = 24) were injured with controlled cortical impact and divided into 3 groups. The first 2 groups were treated with simvastatin (0.5 or 1.0 mg/kg) administered orally for 14 days starting 1 day after TBI. The third group (control) received phosphate-buffered saline orally for 14 days. Neurological functional outcome was measured with modified neurological severity scores performed 1 day before TBI; on days 1, 4, 7, 14 after TBI; and biweekly thereafter. All animals were sacrificed 3 months after TBI. Brain tissues of half of the animals were processed for preparation of paraffin-embedded sections for immunohistological studies. The remaining half were frozen for enzyme-linked immunosorbent assay studies for quantification of brain-derived neurotrophic factor (BDNF) in the hippocampus and cortex. RESULTS: The results showed that both doses of simvastatin significantly improved functional outcome compared with the control, with no difference between the 2 doses. Simvastatin treatment of 1.0 mg/kg increased the number of morphologically intact neurons in the hippocampus, but treatment of 0.5 mg/kg had no significant effect. Enzyme-linked immunosorbent assay studies showed that 0.5 mg/kg simvastatin significantly increased BDNF levels within the hippocampus, but 1.0 mg/kg had no significant effect. Neither dose had any effect on BDNF levels within the cortex. CONCLUSION: Simvastatin treatment provides long-lasting functional improvement after TBI in rats. It also enhances neuronal survival in the hippocampus and increases BDNF levels in the hippocampus secondary to simvastatin treatment.

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Neurosurgery

Paz, N., E. Levanon, E. G. A. Ninette, A. B. Heimberger, Z. Ram, S. Constantini, M. Krupsky, I. Ben-Dov, G. C. Brodie, E. Eisenberg and G. Rechavi (2009). "RNA editing as an epigenetic mechanism contributing to the tumor phenotype." *Febs Journal* **276**: 382-382. [Article Request Form](#)

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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." Journal of Neuro-Oncology **94**(1): 63-68.

[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

Xiong, Y., M. Chopp and C. P. Lee (2009). "Erythropoietin improves brain mitochondrial function in rats after traumatic brain injury." Neurological Research **31**(5): 496-502. [Article](#)

[Request Form](#)

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Lee, CP, Wayne State Univ, Sch Med, Dept Biochem & Mol Biol, Detroit, MI 48201 USA. cplee@med.wayne.edu

Mitochondria play a central role in cellular energetics, calcium homeostasis and apoptosis. Our previous study demonstrates traumatic brain injury induces brain mitochondrial dysfunction after injury. Preservation and/or restoration of mitochondrial function may be one of the strategies for neuroprotection. Erythropoietin, a hormone for erythropoiesis, also provides tissue protection against traumatic brain injury and stroke. The present study was undertaken to evaluate the effect of erythropoietin on traumatic brain injury-induced brain mitochondrial dysfunction. Traumatic brain injury decreased rates of respiration at the active state (state 3), increased that at the resting state (state 4) and consequently decreased respiratory control index (state 3/state 4 ratio) and the efficiency of ATP synthesis (the amount of ADP phosphorylated by inorganic phosphate divided by the amount of oxygen consumed during state 3 respiration). Erythropoietin administered intraperitoneally 30 minutes post-injury at 1000 U/kg partially improved mitochondrial function at day 1 post-injury. However, erythropoietin-induced improvement was not sustained at day 7 post-injury. Erythropoietin at 2000 or 5000 U/kg restored states 3 and 4 examined at day 1 post-injury to the sham levels. Consequently, the energy coupling capacities, such as respiratory control index and/or the efficiency of ATP synthesis, were also improved. The beneficial effect of erythropoietin at these doses persisted for at least 7 days post-injury. The beneficial effect of erythropoietin on brain mitochondrial function was observed with a wide therapeutic window from 5 minutes to 6 hours post-injury. Our data, for the first time, demonstrate that erythropoietin treatment restores brain mitochondrial function after traumatic brain injury, which will enhance cellular energy generation and reduce oxidative stress, strongly supporting erythropoietin as a promising agent for the therapeutic treatment of traumatic brain injury. [Neurol Res 2009; 31: 496-502]

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Other

Aikens, J. E., D. W. Perkins, B. Lipton and J. D. Piette (2009). "Longitudinal Analysis of Depressive Symptoms and Glycemic Control in Type 2 Diabetes." Diabetes Care **32**(7): 1177-1181. [PDF Full-Text](#)

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OBJECTIVE - To compare whether depressive symptoms are more strongly related to subsequent or prior glycemic control in type 2 diabetes and to test whether patient characteristics modify these longitudinal associations. **RESEARCH DESIGN AND METHODS** - On two occasions separated by 6 months, depressive symptoms and glycemic control were assessed in 253 adults with type 2 diabetes. Regression analyses examined depressive symptoms as both a predictor and outcome of glycemic control and tested whether medication regimen (e.g., insulin versus oral drugs) was an effect modifier before and after adjusting for baseline levels of the outcome being predicted. **RESULTS** - Depressive symptom severity predicted poor glycemic control 6 months later ($P = 0.018$) but not after baseline glycemic control was taken into account ($P = 0.361$). Although baseline glycemic control did not generally predict depressive symptoms 6 months later ($P = 0.558$), it significantly interacted with regimen ($P = 0.008$). Specifically, glycemic control predicted depressive symptoms among patients prescribed insulin (beta = 0.31, $P = 0.002$) but not among those prescribed oral medication alone (beta = -0.10, $P = 0.210$). Classifying depression dichotomously produced similar but weaker findings. **CONCLUSIONS** - Depressive Symptoms do not necessarily lead to worsened glycemic control. In contrast, insulin-treated patients in poor glycemic control are at moderate risk, for worsening of depressive symptoms. These patients should be carefully monitored to determine whether depression treatment should be initiated or intensified.

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Other

Brown, S. L., A. Rodger and C. G. Orton (2009). "Point/Counterpoint. Hypofractionation is a proven safe and effective modality for postoperative whole-breast radiotherapy for early breast cancer patients." Med Phys **36**(6): 1927-30. [Article Request Form](#)

Henry Ford Hospital and Wayne State University School of Medicine, Detroit, Michigan 48202-2689, USA. sbrown1@hfhs.org

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Pathology

Lee, H., A. M. Carlin, A. H. Ormsby and M. W. Lee (2009). "Brown Bowel Syndrome Secondary to Jejunioleal Bypass: The First Case Report." Obesity Surgery **19**(8): 1176-1179. [PDF Full-Text](#)

[Lee, Hwajeong; Ormsby, Adrian H.; Lee, Min W.] Henry Ford Hosp, Dept Pathol & Lab Med, Detroit, MI 48202 USA. [Carlin, Arthur M.] Henry Ford Hosp, Dept Surg, Detroit, MI 48202 USA. Lee, H, Henry Ford Hosp, Dept Pathol & Lab Med, 2799 W Grand Blvd, Detroit, MI 48202 USA. hwajeong@gmail.com

A 58-year-old woman with a surgical history of jejunioleal bypass in 1980 for weight reduction sought medical attention with multiple complaints. The patient had not been taking any nutritional supplements since her bypass surgery, 26 years previously. She was found to have osteomalacia, chronic diarrhea, secondary hyperparathyroidism, and hyperoxaluria with a frequent history of nephrolithiasis. Because of her severe osteodystrophy and metabolic complications, reversal of her jejunioleal bypass was recommended. Reversal of the jejunioleal bypass with a sleeve gastrectomy was performed. Laparotomy revealed brown discoloration of the entire alimentary limb with atrophy of the bypassed intestinal limb. Histologic examination of the resected small bowel demonstrated brown pigment deposits within smooth muscle cells of the bowel wall. The pigment stained positive with Fontana-Masson most likely representing lipofuscin. We report a case of brown bowel syndrome complicating jejunioleal bypass, the first case reported in the literature to the best of our knowledge.

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Pathology

Lehman, N. L. (2009). "The ubiquitin proteasome system in neuropathology." Acta Neuropathol **118**(3): 329-47. PMC2716447. [PDF Full-Text](#)

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The ubiquitin proteasome system (UPS) orchestrates the turnover of innumerable cellular proteins. In the process of ubiquitination the small protein ubiquitin is attached to a target protein by a peptide bond. The ubiquitinated target protein is subsequently shuttled to a protease complex known as the 26S proteasome and subjected to degradative proteolysis. The UPS facilitates the turnover of proteins in several settings. It targets oxidized, mutant or misfolded proteins for general proteolytic destruction, and allows for the tightly controlled and specific destruction of proteins involved in development and differentiation, cell cycle progression, circadian rhythms, apoptosis, and other biological processes. In neuropathology, alteration of the UPS, or mutations in UPS target proteins may result in signaling abnormalities leading to the initiation or progression of tumors such as astrocytomas, hemangioblastomas, craniopharyngiomas, pituitary adenomas, and medulloblastomas. Dysregulation of the UPS may also contribute to tumor progression by perturbation of DNA replication and mitotic control mechanisms, leading to genomic instability. In neurodegenerative diseases caused by the expression of mutant proteins, the cellular accumulation of these proteins may overload the UPS, indirectly contributing to the disease process, e.g., sporadic Parkinsonism and prion diseases. In other cases, mutation of UPS components may directly cause pathological accumulation of proteins, e.g., autosomal recessive Parkinsonism and spinocerebellar ataxias. Defects or dysfunction of the UPS may also underlie cognitive disorders such as Angelman syndrome, Rett syndrome and autism, and muscle and nerve diseases, e.g., inclusion body myopathy and giant axon neuropathy. This paper describes the basic biochemical mechanisms comprising the UPS and reviews both its theoretical and proven involvement in neuropathological diseases. The potential for the UPS as a target of pharmacological therapy is also discussed.

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Pathology

Sharma, G., R. K. Shamanna, C. S. Feldkamp, J. Zajechowski and M. Cosman (2009). "Analytical Performance of Dimension Vista (R) Vitamin B12 (B12) and Folate (FOL) methods using LOCI (R) Technology." Clinical Chemistry **55**(6): A231-A232. [Article Request Form](#)

[Sharma, G.; Shamanna, R. Kanagal; Feldkamp, C. S.; Zajechowski, J.; Cosman, M.] Henry Ford Hosp, Detroit, MI 48202 USA.

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Pathology

Stapp, R., J. Zajechowski, C. Feldkamp, L. Stezar, W. Beher, J. Carey and V. I. Luzzi (2009). "Discordant Results Between the Siemens Advia Centaur (R) Hepatitis B Core IgM and Clinical Findings." Clinical Chemistry **55**(6): A145-A145. [Article Request Form](#)

[Stapp, R.; Zajechowski, J.; Feldkamp, C.; Stezar, L.; Beher, W.; Carey, J.; Luzzi, V. I.] Henry Ford Med Labs, Detroit, MI USA.

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Pathology

Zajechowski, J., C. Feldkamp, M. Cosman, J. Carey and V. Luzzi (2009). "Analytical Performance of a Non-extraction Cyclosporine Immunoassay in the Siemens Dimension Vista (R)." Clinical Chemistry **55**(6): A256-A256. [Article Request Form](#)

[Zajechowski, J.; Feldkamp, C.; Cosman, M.; Carey, J.; Luzzi, V.] Henry Ford Med Labs, Detroit, MI USA.

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Pulmonary & Critical Care Medicine

Jennings, J. H., B. Digiovine, D. Obeid and C. Frank (2009). "The association between depressive symptoms and acute exacerbations of COPD." Lung **187**(2): 128-35. [PDF Full-Text](#)

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BACKGROUND: Depression is an important comorbidity for patients with chronic obstructive pulmonary disease (COPD). The association between depression and acute exacerbations of COPD is unknown. This study was designed to determine the frequency of COPD exacerbations in outpatients with and without depressive symptoms. **METHODS:** In this retrospective cohort study, patients with a primary diagnosis of COPD were followed for 1 year after discharge from a pulmonary rehabilitation program and the frequency of exacerbations was recorded. Upon completion of the program, all patients were administered the Short-Form 36 Health Survey (SF-36), which contains a mental health domain. Patients were classified as having depressive symptoms based on their domain score, which was separately validated in a second population of patients. **RESULTS:** Of the 194 patients with COPD who completed the pulmonary rehabilitation program, 32 (16.5%) had depressive symptoms. There were no differences in terms of age, race, pack-years, forced expiratory volume in 1 second (FEV(1)), 6-minute walk distance, body mass index, use of supplemental oxygen, use of inhaled steroids, or the Charlson Comorbidity Index between patients with and without depressive symptoms. Patients with depressive symptoms had more exacerbations in the following year (1.91 vs. 1.36; $p = 0.02$), were 2.8 times more likely to have ever had an exacerbation (95% confidence interval (CI), 1.1-7.3; $p = 0.03$), and suffered a first exacerbation earlier (148 days compared with 266 days; $p = 0.04$) than nondepressed patients. **CONCLUSIONS:** COPD patients with depressive symptoms have a significantly higher risk for exacerbations. Early screening for depression in patients with COPD may help identify those patients at higher risk for subsequent exacerbations.

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Radiation Oncology

Jin, J. Y., F. M. Kong, I. J. Chetty, M. Ajlouni, S. Ryu, R. Ten Haken and B. Movsas (2009). "Impact of Fraction Size on Lung Radiation Toxicity: Hypofractionation May Be Beneficial in Dose Escalation of Radiotherapy for Lung Cancers." Int J Radiat Oncol Biol Phys. EPub Ahead of Print. [PDF Full-Text](#)

Department of Radiation Oncology, Henry Ford Hospital, Detroit, MI.

PURPOSE: To assess how fraction size impacts lung radiation toxicity and therapeutic ratio in treatment of lung cancers. **METHODS AND MATERIALS:** The relative damaged volume (RDV) of lung was used as the endpoint in the comparison of various fractionation schemes with the same normalized total dose (NTD) to the tumor. The RDV was computed from the biologically corrected lung dose-volume histogram (DVH), with an alpha/beta ratio of 3 and 10 for lung and tumor, respectively. Two different (linear and S-shaped) local dose-effect models that incorporated the concept of a threshold dose effect with a single parameter $D(L50)$ (dose at 50% local dose effect) were used to convert the DVH into the RDV. The comparison was conducted using four representative DVHs at different NTD and $D(L50)$ values. **RESULTS:** The RDV decreased with increasing dose/fraction when the NTD was larger than a critical dose ($D(CR)$) and increased when the NTD was less than $D(CR)$. The $D(CR)$ was 32-50 Gy and 58-87 Gy for a small tumor (11 cm³) for the linear and S-shaped local dose-effect models, respectively, when $D(L50)$ was 20-30 Gy. The $D(CR)$ was 66-97 Gy and 66-99 Gy, respectively, for a large tumor (266 cm³). Hypofractionation was preferred for small tumors and higher NTDs, and conventional fractionation was better for large tumors and lower NTDs. Hypofractionation might be beneficial for intermediate-sized tumors when $NTD = 80-90$ Gy, especially if the $D(L50)$ is small (20 Gy). **CONCLUSION:** This computational study demonstrated that hypofractionated stereotactic body radiotherapy is a better regimen than conventional fractionation in lung cancer patients with small tumors and high doses, because it generates lower RDV when the tumor NTD is kept unchanged.

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Radiation Oncology

Peck, D. (2009). "Digital Imaging and Communications in Medicine (DICOM): A Practical Introduction and Survival Guide." J Nucl Med. EPub Ahead of Print. [PDF Full-Text](#)

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Radiation Oncology

Shepard, S. J., J. H. Wang, M. Flynn, E. Gingold, L. Goldman, K. Krugh, D. L. Leong, E. Mah, K. Ogden, D. Peck, E. Samei and C. E. Willis (2009). "An exposure indicator for digital radiography: AAPM Task Group 116 (Executive Summary)." Medical Physics **36**(7): 2898-2914.

[Article Request Form](#)

[Shepard, S. Jeff; Wang, Jihong] Univ Texas MD Anderson Canc Ctr, Imaging Phys Dept 056, Div Diagnost Imaging, Houston, TX 77030 USA. [Flynn, Michael] Henry Ford Hlth Syst, Dept Radiol, Radiol Res 2F, Detroit, MI 48202 USA. [Gingold, Eric] Thomas Jefferson Univ Hosp, Dept Radiol, Philadelphia, PA 19107 USA. [Goldman, Lee] Hartford Hosp, Dept Med Phys, Hartford, CT 06102 USA. [Krugh, Kerry] Toledo Hosp, Dept Radiol, Toledo, OH 43606 USA. [Leong, David L.] Analogic Corp, Peabody, MA 01960 USA. [Mah, Eugene] Med Univ S Carolina, Dept Radiol, Charleston, SC 29425 USA. [Ogden, Kent] SUNY Upstate Med Univ, Dept Radiol, Syracuse, NY 13210 USA. [Peck, Donald] Henry Ford Hosp, Detroit, MI 48202 USA. [Samei, Ehsan] Duke Univ, Med Ctr, Radiol Med Phys Phys & BME, Durham, NC 27705 USA. [Willis, Charles E.] Univ Texas MD Anderson Canc Ctr, Imaging Phys Dept, Houston, TX 77030 USA.

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Digital radiographic imaging systems, such as those using photostimulable storage phosphor, amorphous selenium, amorphous silicon, CCD, and MOSFET technology, can produce adequate image quality over a much broader range of exposure levels than that of screen/film imaging systems. In screen/film imaging, the final image brightness and contrast are indicative of over- and underexposure. In digital imaging, brightness and contrast are often determined entirely by digital postprocessing of the acquired image data. Overexposure and underexposures are not readily recognizable. As a result, patient dose has a tendency to gradually increase over time after a department converts from screen/film-based imaging to digital radiographic imaging. The purpose of this report is to recommend a standard indicator which reflects the radiation exposure that is incident on a detector after every exposure event and that reflects the noise levels present in the image data. The intent is to facilitate the production of consistent, high quality digital radiographic images at acceptable patient doses. This should be based not on image optical density or brightness but on feedback regarding the detector exposure provided and actively monitored by the imaging system. A standard beam calibration condition is recommended that is based on RQA5 but uses filtration materials that are commonly available and simple to use. Recommendations on clinical implementation of the indices to control image quality and patient dose are derived from historical tolerance limits and presented as guidelines.

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Radiation Oncology

Siddiqui, F., M. Patel, M. Khan, S. McLean, J. Dragovic, J. Y. Jin, B. Movsas and S. Ryu (2009). "Stereotactic Body Radiation Therapy for Primary, Recurrent, and Metastatic Tumors in the Head-and-Neck Region." International Journal of Radiation Oncology Biology Physics **74**(4): 1047-1053. [PDF Full-Text](#)

[Siddiqui, Farzan; Patel, Mehul; Dragovic, Jadranka; Jin, Jian-Yue; Movsas, Benjamin; Ryu, Samuel] Henry Ford Hlth Syst, Dept Radiat Oncol, Detroit, MI 48202 USA. [Khan, Mumtaz; McLean, Scott] Henry Ford Hlth Syst, Dept Otolaryngol Head & Neck Surg, Detroit, MI 48202 USA.

Ryu, S, Henry Ford Hlth Syst, Dept Radiat Oncol, 2799 W Grand Blvd, Detroit, MI 48202 USA. sryu1@hfhs.org

Purpose: To determine the feasibility, safety, and efficacy of stereotactic body radiation therapy (SBRT), also known as radiosurgery, in patients with head-and-neck cancers. Methods and Materials: Patients with pathologically proven malignant lesions in the head-and-neck region were treated using single-dose SBRT (S-SBRT) or fractionated SBRT (F-SBRT). Radiation doses were either single-fraction 13-18 Gy for S-SBRT or 36-48 Gy in five to eight fractions for F-SBRT. Response evaluation was based on clinical examinations and computed tomography/magnetic resonance imaging scans. Pre- and post-SBRT tumor dimensions were measured in three axes, and tumor volumes were calculated. Response evaluation also was performed using World Health Organization criteria. Results: Fifty-five lesions were treated in 44 patients (25 men, 19 women). There were three groups of patients: those with primary (n = 10), recurrent (n = 21), and metastatic tumors (n = 13). The predominant histologic type was squamous cell carcinoma (n = 33). The majority of lesions were treated using F-SBRT (n = 37). Based on radiographic and clinical assessment, a 77% (complete + partial response) response rate

was noted. Percentage of reduction in tumor volume was 52% 38% based on follow-up scans in 24 patients. Tumor control rates at 1 year were 83.3% and 60.6% in the primary and recurrent groups, respectively. Median overall survival was 28.7, 6.7, and 5.6 months for the primary, recurrent, and metastatic groups, respectively. Radiation Therapy Oncology Group Grade 1-2 mucositis was noted in all patients treated for oropharyngeal or laryngeal lesions. Conclusions: The SBRT in single or fractionated doses offers a viable treatment option for selected patients with primary, recurrent, and metastatic head-and-neck cancers with functional preservation. (C) 2009 Elsevier Inc.

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Sleep Medicine

Richardson, G. S., G. Zammit, S. Wang-Weigand and J. Zhang (2009). "Safety and subjective sleep effects of ramelteon administration in adults and older adults with chronic primary insomnia: a 1-year, open-label study." J Clin Psychiatry **70**(4): 467-76. [PDF Full-Text](#)

Henry Ford Hospital, Sleep Disorders Center, Detroit, MI 48202, USA. gsr@attglobal.net

OBJECTIVE: To evaluate the long-term safety and subjective sleep effects of ramelteon in adults with chronic insomnia. METHOD: Subjects with primary insomnia (DSM-IV-TR criteria) for ≥ 3 months received ramelteon nightly for 1 year; a 3-day placebo run out followed. Subjects aged ≥ 65 years received open-label ramelteon 8 mg (N = 248); those aged 18 to 64 years received ramelteon 16 mg (N = 965). Subjects completed sleep diaries and returned to the clinic at week 1 and at months 1, 2, 3, 4, 6, 8, 10, and 12 for safety assessments and investigator-performed Clinical Global Impressions. The study was conducted from February 2003 through September 2004. RESULTS: There were no noteworthy changes in vital signs, physical examinations, clinical chemistry, hematology, or urinalysis values and no electrocardiogram changes to suggest adverse cardiac effects. Endocrine values remained within normal range throughout treatment. Consistent statistically significant ($p < 0.05$) decreases in free thyroxine (in adults) and free testosterone (in older men) were detected. Duration of menses increased by approximately 1 day. A total of 40.8% of subjects reported at least 1 adverse event possibly associated with ramelteon use. The adverse events reported varied considerably, the incidence of individual adverse events was low, and the frequencies of adverse events were similar at months 6 and 12. In both groups, subjective sleep latency and total sleep time improved by month 1 and was sustained during the 1-year period. At 6 months and 1 year, Clinical Global Impressions indices were improved. During placebo run out, subjective sleep latency did increase but did not return to baseline. CONCLUSION: Year-long administration of ramelteon was well tolerated. Ramelteon was associated with sustained improvements in subjective sleep latency, subjective total sleep time, and Clinical Global Impressions. TRIAL REGISTRATION: clinicaltrials.gov Identifier: NCT00671086.

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Sleep Medicine

Roth, T. (2009). "Sleep duration, insomnia and longevity." Sleep Med. Epub Ahead of Print. [PDF Full-Text](#)

Sleep Disorders and Research Center, Henry Ford Hospital, 2799 W Grand Blvd, CFP-3, Detroit, MI 48202, USA.

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Sleep Medicine

Staner, L., M. Eriksson, F. Cornette, F. Santoro, N. Muscat, R. Luthinger and T. Roth (2009). "Sublingual zolpidem is more effective than oral zolpidem in initiating early onset of sleep in the post-nap model of transient insomnia: A polysomnographic study." Sleep Medicine **10**(6): 616-620. [PDF Full-Text](#)

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Objective: OX22 is zolpidem formulated for sublingual administration. The primary objective of the present study was to evaluate the efficacy of single doses of sublingual zolpidem (5 and 10 mg) versus oral zolpidem (10 mg), with regard to latency to persistent sleep (LPS), in a post-nap model of insomnia. Methods: Twenty-one healthy volunteers included in this study were recorded by polysomnography during 2 consecutive nights and, on the day

in between, during a 2 h nap. Eighteen out of these 21 subjects were finally analyzed. Treatment was randomly administered before the second recording night to subjects demonstrating at least 30 min of sleep during the nap recording. Results: Contrast analyses show that 10 mg OX22 significantly shortened LPS compared to oral zolpidem administration of 10 mg (12.8 +/- 9.9 and 18.4 +/- 11.3 min, respectively; $p < .05$). No treatment effects could be evidenced on total sleep time, time awake after sleep onset and sleep architecture parameters for OX22 compared to oral zolpidem. All treatments were well tolerated and did not induce next-day residual effects. Conclusion: The present results show that OX22, a sublingual formulation of zolpidem, has a significant earlier sleep initiation as compared to an equivalent dose of oral zolpidem in healthy volunteers in a post-nap model of insomnia. (c) 2008 Elsevier B.V. All rights reserved.

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Surgery

Abou Abbass, A., A. Yoshida, R. Slater, M. Abouljoud, D. Kim, D. Moonka, M. Kazimi and J. Hundley (2009). "Biliary Complications after Orthotopic Liver Transplantation from Donors after Cardiac Death: Spectrum of Disease." Liver Transplantation **15**(7): S80-S81. [PDF Full-Text](#)

[Abou Abbass, Ahmad; Yoshida, Atsushi; Slater, Rob; Abouljoud, Marwan; Kim, Dean; Kazimi, Marwan; Hundley, John] Henry Ford Hlth Syst, Transplant & Hepatobiliary Surg, Detroit, MI USA. [Moonka, Dilip] Henry Ford Hlth Syst, Hepatol, Detroit, MI USA.

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Surgery

Jones, J. A., A. E. Sargsyan, Y. R. Barr, S. Melton, D. R. Hamilton, S. A. Dulchavsky and P. A. Whitson (2009). "Diagnostic Ultrasound at Mach 20: Retroperitoneal and Pelvic Imaging in Space." Ultrasound in Medicine and Biology **35**(7): 1059-1067. [Article Request Form](#)

[Jones, J. A.] NASA, Lyndon B Johnson Space Ctr, JSC SD2, Space Med & Hlth Care Syst Med Operat Branch, Houston, TX 77058 USA. [Jones, J. A.] Int Space Univ, Strasbourg, France. [Sargsyan, A. E.; Melton, S.; Hamilton, D. R.] Wyle Integrated Sci & Engrn Grp, Houston, TX USA. [Barr, Y. R.] Univ Texas Med Branch, Dept Prevent Med Aerosp Med, Galveston, TX USA. [Dulchavsky, S. A.] Henry Ford Hosp, Dept Surg, Detroit, MI 48202 USA. Jones, JA, NASA, Lyndon B Johnson Space Ctr, JSC SD2, Space Med & Hlth Care Syst Med Operat Branch, 2101 NASA Pkwy, Houston, TX 77058 USA. jeffrey.a.jones@nasa.gov

An operationally available diagnostic imaging capability augments spaceflight medical support by facilitating the diagnosis, monitoring and treatment of medical or surgical conditions, by improving medical outcomes and, thereby, by lowering medical mission impacts and the probability of crew evacuation due to medical causes. Microgravity-related physiological changes occurring during spaceflight can affect the genitourinary system and potentially cause conditions such as urinary retention or nephrolithiasis for which ultrasonography (U/S) would be a useful diagnostic tool. This study describes the first genitourinary ultrasound examination conducted in space, and evaluates image quality, frame rate, resolution requirements, real-time remote guidance of nonphysician crew medical officers and evaluation of on-orbit tools that can augment image acquisition. A nonphysician crew medical officer (CMO) astronaut, with minimal training in U/S, performed a self-examination of the genitourinary system onboard the International Space Station, using a Philips/ATL Model HDI-5000 ultrasound imaging unit located in the International Space Station Human Research Facility. The CMO was remotely guided by voice commands from experienced, earth-based sonographers stationed in Mission Control Center in Houston. The crewmember, with guidance, was able to acquire all of the target images. Real-time and still U/S images received at Mission Control Center in Houston were of sufficient quality for the images to be diagnostic for multiple potential genitourinary applications. Microgravity-based ultrasound imaging can provide diagnostic quality images of the retroperitoneum and pelvis, offering improved diagnosis and treatment for onboard medical contingencies. Successful completion of complex sonographic examinations can be obtained even with minimally trained nonphysician ultrasound operators, with the assistance of ground-based real-time guidance. (E-mail: jeffrey.a.jones@nasa.gov) Published by Elsevier Inc. on behalf of World Federation for Ultrasound in Medicine & Biology.

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Surgery

Tsiouris, A., A. Kourliouros and E. E. J. Smith (2009). "Trends and challenges in treatment of malignant pleural mesothelioma." British Journal of Hospital Medicine **70**(6): 312-313. [Article Request Form](#)

[Tsiouris, Athanasios] Henry Ford Hosp, Detroit, MI 48202 USA. [Kourliouros, Antonios; Smith, E. E. John] Univ London St Georges Hosp, Dept Cardiothorac Surg, London, England.
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Surgery

Velanovich, V., I. Rubinfeld, J. H. Patton, Jr., J. Ritz, J. Jordan and S. Dulchavsky (2009). "Implementation of the National Surgical Quality Improvement Program: Critical Steps to Success for Surgeons and Hospitals." Am J Med Qual. Epub Ahead of Print. [Article Request Form](#)

Henry Ford Hospital, Detroit, Michigan.

The National Surgical Quality Improvement Program (NSQIP), as administered by the American College of Surgeons, became available to private sector hospitals across the United States in 2004. The program works to improve surgical outcomes by providing high-quality, risk-adjusted data to surgeons at a given hospital to stimulate discussion and define target areas for improvement. Although the NSQIP began in the early 1990s with Veterans Administration hospitals and expanded to private sector hospitals nearly 5 years ago, the "how to" process for NSQIP implementation has been left to individual institutions to manage on their own. The NSQIP was instituted at a large tertiary hospital in 2005, identifying through experience 12 critical steps to help surgeons and hospitals implement the NSQIP. (Am J Med Qual 2009;24:xx-xx).

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Urology

Gupta, A., M. Dwivedi, A. A. Mahdi, G. N. Gowda, C. L. Khetrpal and M. Bhandari (2009). "H-1-nuclear magnetic resonance spectroscopy for identifying and quantifying common uropathogens: a metabolic approach to the urinary tract infection." Bju International **104**(2): 236-244. [PDF Full-Text](#)

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Bhandari, M, K 9 Henry Ford Hosp, Vattikuti Urol Inst, 2799 W Grand Blvd, Detroit, MI USA. mbhanda1@hfhs.org

OBJECTIVE To address the shortcomings of urine culture for the diagnosis of urinary tract infection (UTI), we used H-1-nuclear magnetic resonance (NMR) spectroscopy for identifying and quantifying *Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae* and *Proteus mirabilis*. **PATIENTS, SUBJECTS AND METHODS** Urine samples from patients with suspected UTI (617), healthy volunteers (50) and commercially available standard strains of *E. coli*, *K. pneumoniae*, *P. aeruginosa*, *Enterobacter*, *Acinobacter*, *Pr. mirabilis*, *Citrobacter freundii*, *Streptococcus saprophyticus* and *Enterococcus faecalis* were assessed between 2003 and 2006. H-1-NMR spectra were recorded on a 400 MHz spectrophotometer; to quantify the bacteria we estimated the areas under the spectral peaks of the specific metabolic product compared with the known concentration of trimethyl silyl propionic acid. All urine specimens were cultured in addition to an assessment by NMR spectroscopy. **RESULTS** Preliminary urinary spectroscopy of the unprocessed samples showed peaks of nonspecific metabolites such as succinate, acetate, lactate and ethanol, indicating infected samples. Based on the results from processed samples, 93% (240/256) of *E. coli*, 92% (101/110) of *K. pneumoniae*, 93% (56/60) of *P. aeruginosa* and eight of 10 *Pr. mirabilis* could be diagnosed with NMR (numerator) and urine culture (denominator). The remaining samples were sterile and/or had a bacterial population of < 10³ colony-forming units (CFU)/mL. The NMR method diagnosed bacterial densities of > 10³ CFU. **CONCLUSIONS** The identification of the common uropathogens *E. coli*, *K. pneumoniae*, *P. aeruginosa* and *Pr. mirabilis* by NMR spectroscopy has a shorter reporting time and can be used to differentiate between infected, contaminated and sterile specimens.

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Urology

Krane, L. S., M. Menon, S. A. Kaul, S. A. Siddiqui, C. Wambi, J. O. Peabody and P. K. Agarwal (2009). "Role of PSA velocity in predicting pathologic upgrade for Gleason 6 prostate cancer." Urol Oncol. EPub Ahead of Print. [PDF Full-Text](#)

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BACKGROUND: Pathologic upgrading to Gleason 7 or higher on radical prostatectomy (RP) specimens occurs in many patients with Gleason 6 prostate cancer on preoperative biopsy. We evaluated whether biopsy characteristics and preoperative factors, including preoperative PSA velocity (PSAV), are predictive of pathologic upgrading. **MATERIALS AND METHODS:** We identified 235 consecutive Gleason 6 prostate cancer patients who underwent biopsies at our institution, had multiple pre-biopsy PSA values, and eventually underwent RP. Preoperative biopsy, clinical characteristics, and PSAV were analyzed to determine the risk of pathologic upgrading or extracapsular extension. These clinical factors were evaluated for association with biochemical recurrence following RP. **RESULTS:** Overall, 48% of patients were upgraded to Gleason grade 7 or higher following RP. Median PSAV was 0.61 ng/mL/y, and PSAV was similar between upgraded and non-upgraded patients (1.01 vs. 0.78, $P = 0.1$). PSA velocity level was not associated with extracapsular disease ($P = 0.4$). PSA velocity > 1 was associated with biochemical recurrence (HR 3.23, $P = 0.01$) but this was not statistically significant in a multivariable model. Increasing PSA density (HR 2.18, $P < 0.001$), bilateral cores positive (HR 1.89, $P < 0.05$), and any biopsy core involvement $> 50\%$ (HR 2.52, $P < 0.05$) were most associated with pathologic upgrading. On multivariate analysis, only bilateral cancer detection at biopsy (HR 1.90, $P < 0.05$) significantly predicted upgrading. **CONCLUSIONS:** PSAV has a limited role in predicting Gleason 6 upgrading. Patients with bilateral cancer detected on transrectal biopsy should be encouraged to have radical local therapy due to high risk of harboring more aggressive disease.

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Urology

Menon, M., A. Shrivastava, M. Bhandari, R. Satyanarayana, S. Siva and P. K. Agarwal (2009). "Vattikuti Institute Prostatectomy: Technical Modifications in 2009." European Urology **56**(1): 89-96. [PDF Full-Text](#)

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Background: Since we last published our technique of robotic prostatectomy, we have introduced three technical refinements: superviseil nerve sparing, bladder drainage with a percutaneous suprapubic tube (PST), and limited node dissection of the obturator and internal iliac nodes in preference to the external iliac nodes in selected patients. **Objective:** To describe selection criteria, to explain the three techniques, and to evaluate functional and oncologic results. **Design, setting, and participants:** Single-institution study of 1151 radical prostatectomies performed from 2006 to 2008 by one surgeon. **Surgical procedure:** The superviseil nerve-sparing technique spares nerves from the 11-o'clock position to the 1-o'clock position. The bladder is drained with a PST rather than a urethral catheter. For low- of intermediate-risk disease, limited lymphadenectomy concentrates on the internal iliac and obturator nodes, excluding the external iliac lymph nodes. **Measurements:** Erectile function and patient comfort were evaluated using questionnaires administered by a third party. Lymph node yield was quantified by a qualified uropathologist. **Results and limitations:** At 6-18 months after surgery, 94% of men who attempted sexual intercourse were successful with a median Sexual Health Inventory For Men (SHIM) score of 18 out of 25. PST bladder drainage resulted in less patient discomfort; Visual analog scores were 2 at 2 days after prostatectomy and 0 at 6 days after prostatectomy. The modified lymphadenectomy harvested few overall nodes, but it increased the yield of positive nodes >13 -fold in patients with low-risk stratification (6.7% compared with 0.5%). **Conclusion:** In this single-institution, single-surgeon study, these modifications improved erectile function outcomes, decreased catheter-associated discomfort, and enhanced the detection of positive nodes.

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Urology

Rogers, C. G. and J. J. Patard (2009). "The Motion: Robotic Partial Nephrectomy is Better than Open Partial Nephrectomy." Eur Urol. EPub Ahead of Print. [PDF Full-Text](#)

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