

## Henry Ford Health System Publication List June 2009

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### Administration

Kelley, M. (2009). "Meet Mark Kelley, MD, CEO of the Henry Ford Medical Group. Interviews by Paul Natinsky." Mich Med **108**(3): 14-5. [Article Request Form](#)

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### Biostatistics & Research Epidemiology

Croswell, J. M., B. S. Kramer, A. R. Kreimer, P. C. Prorok, J. L. Xu, S. G. Baker, R. Fagerstrom, T. L. Riley, J. D. Clapp, C. D. Berg, J. K. Gohagan, G. L. Andriole, D. Chia, T. R. Church, E. D. Crawford, M. N. Fouad, E. P. Gelmann, L. Lamerato, D. J. Reding and R. E. Schoen (2009).

"Cumulative Incidence of False-Positive Results in Repeated, Multimodal Cancer Screening." Annals of Family Medicine **7**(3): 212-222. [PDF Full-Text](#)

[Croswell, Jennifer Miller; Kramer, Barnett S.] NIH, Off Director, Off Dis Prevent, Bethesda, MD 20892 USA. [Kreimer, Aimee R.; Xu, Jian-Lun; Baker, Stuart G.; Fagerstrom, Richard; Berg, Christine D.; Gohagan, John K.] NIH, Natl Canc Inst, Canc Prevent Div, Bethesda, MD 20892 USA. [Riley, Thomas L.; Clapp, Jonathan D.] IMS Inc, Washington, DC USA. [Andriole, Gerald L.] Washington Univ, Sch Med, St Louis, MO USA. [Chia, David] Univ Calif Los Angeles, Sch Med, Los Angeles, CA USA. [Church, Timothy R.] Univ Minnesota, Sch Publ Hlth, Minneapolis, MN USA. [Crawford, E. David] Univ Colorado, Hlth Sci Ctr, Aurora, CO USA. [Fouad, Mona N.] Univ Alabama, Birmingham, AL USA. [Gelmann, Edward P.] Columbia Univ, Herbert Irving Comprehens Canc Ctr, New York, NY USA. [Lamerato, Lois] Henry Ford Hlth Syst, Detroit, MI USA. [Reding, Douglas J.] Marshfield Clin Res Fdn, Marshfield, WI USA. [Schoen, Robert E.] Univ Pittsburgh, Sch Med, Pittsburgh, PA USA. Croswell, JM, NIH, Off Director, Off Dis Prevent, 6100 Execut Blvd, Suite 2B-03, Bethesda, MD 20892 USA. [croswellj@od.nih.gov](mailto:croswellj@od.nih.gov)

PURPOSE Multiple cancer screening tests have been advocated for the general population; however, clinicians and patients are not always well-informed of screening burdens. We sought to determine the cumulative risk of a false-positive screening result

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8:30am-5:00pm F

and the resulting risk of a diagnostic procedure for an individual participating in a multimodal cancer screening program. METHODS Data were analyzed from the intervention arm of the ongoing Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial, a randomized controlled trial to determine the effects of prostate, lung, colorectal, and ovarian cancer screening on disease-specific mortality. The 68,436 participants, aged 55 to 74 years, were randomized to screening or usual care. Women received serial serum tests to detect cancer antigen 125 (CA-125), transvaginal sonograms, posteroanterior-view chest radiographs, and flexible sigmoidoscopies. Men received serial chest radiographs, flexible sigmoidoscopies, digital rectal examinations, and serum prostate-specific antigen tests. Fourteen screening examinations for each sex were possible during the 3-year screening period. After 14 tests, the cumulative risk of having at least 1 false-positive screening test is 60.4% (95% CI, 59.8%-61.0%) for men, and 48.8% (95% CI, 48.1%-49.4%) for women. The cumulative risk after 14 tests of undergoing an invasive diagnostic procedure prompted by a false-positive test is 28.5% (CI, 27.8%-29.3%) for men and 22.1% (95% CI, 21.4%-22.7%) for women. CONCLUSIONS For an individual in a multimodal cancer screening trial, the risk of a false-positive finding is about 50% or greater by the 14th test. Physicians should educate patients about the likelihood of false positives and resulting diagnostic interventions when counseling about cancer screening.

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### **Biostatistics & Research Epidemiology**

Havstad, S., E. Zoratti, D. Ownby, C. Johnson and G. Wegienka (2009). "Delivery by cesarian is not related to cord blood IgE or skin prick test results at age 2 years." Allergy **64**: 818. [Article Request Form](#)

[Havstad, S.; Johnson, C.; Wegienka, G.] Henry Ford Hosp, Dept Biostat & Res Epidemiol, Detroit, MI 48202 USA. [Zoratti, E.] Henry Ford Hosp, Dept Allergy & Clin Immunol, Detroit, MI 48202 USA. [Ownby, D.] Med Coll Georgia, Dept Pediat, Augusta, GA 30912 USA.

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### **Biostatistics & Research Epidemiology**

Johnson, D., G. Divine, G. Alexander, S. Rolnick, J. Calvi, M. Stopponi, J. McClure, J. Richards, V. Strecher and C. C. Johnson (2009). "The Role of Family Disease History and Perceived Risk of Disease in Change of Fruit and Vegetable Consumption over 12 Mths." American Journal of Epidemiology **169**: S62-S62. [Article Request Form](#)

[Johnson, D.; Divine, G.; Alexander, G.; Rolnick, S.; Calvi, J.; Stopponi, M.; McClure, J.; Richards, J.; Strecher, V.; Johnson, C. C.] Henry Ford Hlth Syst, Biostat & Res Epi, Detroit, MI USA.

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### **Biostatistics & Research Epidemiology**

Joseph, C. L. M., S. L. Havstad, D. R. Ownby, E. Zoratti, E. L. Peterson, S. Stringer and C. C. Johnson (2009). "Gender differences in the association of overweight and asthma morbidity among urban adolescents with asthma." Pediatric Allergy and Immunology **20**(4): 362-369. [PDF Full-Text](#)

[Joseph, C. L. M.; Havstad, S. L.; Peterson, E. L.; Johnson, C. C.] Henry Ford Hlth Syst, Dept Biostat & Res Epidemiol, Detroit, MI 48202 USA. [Ownby, D. R.] Med Coll Georgia, Augusta, GA 30912 USA. [Stringer, S.] NCI, Appl Res Program, Div Canc Control & Populat Sci, Bethesda, MD 20892 USA.

Joseph, CLM, Henry Ford Hlth Syst, Dept Biostat & Res Epidemiol, 1 Ford Pl,3E, Detroit, MI 48202 USA. [cjoseph1@hfhs.org](mailto:cjoseph1@hfhs.org)

Asthma and obesity disproportionately affect US African-American youth. Among youth with asthma, obesity has been associated with poor control. The impact of gender on this association is unclear. We examined these relationships in a sample of urban, African-American adolescents with asthma. Questionnaires were used to identify high school students with asthma, and to examine the association of body mass index (BMI) to

asthma morbidity, by gender. Of 5967 students completing questionnaires, 599 (10%) met criteria for asthma and 507 had data sufficient for inclusion in further analyses (46% male, mean age = 15.1 yr). Univariately, BMI > 85th percentile was significantly related only to reported emergency department visits (ED) and school days missed for any reason, Odds Ratio (95% Confidence Interval) = 1.7(1.1-2.7),  $p = 0.01$  and 1.8(1.1-3.0),  $p = 0.01$ , respectively. A significant gender-BMI interaction ( $p < 0.05$ ) was observed in multivariate models for ED visits, hospitalizations and school days missed for asthma. In gender-specific models, adjusted Risk Ratios for BMI > 85th and ED visits, hospitalizations, and school days missed because of asthma were 1.7(0.9-3.2), 6.6(3.1-14.6) and 3.6(1.8-7.2) in males. These associations were not observed in females. Gender modifies the association between BMI and asthma-related morbidity among adolescents with asthma. Results have implications for clinical management as well as future research.

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### **Biostatistics & Research Epidemiology**

Wegienka, G., S. Havstad, E. M. Zoratti, K. J. Woodcroft, K. R. Bobbitt, D. R. Ownby and C. C. Johnson (2009). "Regulatory T cells in prenatal blood samples: variability with pet exposure and sensitization." J Reprod Immunol **Epub Ahead of Print**. [Article Request Form](#)

Department of Biostatistics and Research Epidemiology, Henry Ford Hospital, 1 Ford Place, 3E, Detroit, MI 48202, USA.

Fetal exposures have come under investigation as risk factors of early life allergic disease. In this study we aimed to examine the relationships between dog or cat exposure and naturally occurring regulatory T cells (Treg cells), thought to play an important role in immune tolerance, in pregnant women. A cross-sectional analysis was conducted among 204 pregnant women who were queried regarding dog and cat exposure. Treg cells (CD4+CD25+Foxp3+ lymphocytes) and allergen-specific IgE were measured in venous blood samples. Atopy was defined as allergen-specific IgE  $\geq 0.35$  kU/l reactive with common allergens including dust mite, dog, cat, Timothy grass, ragweed, *Alternaria alternata*, egg white or cockroach. Nonparametric Wilcoxon rank sum tests and linear regression models of log transformed Treg cell levels were used in analyses. Among women sensitized to dog, those who had a dog or cat in the home had lower Treg cell levels compared with those who had no dog or cat. However, among women not sensitized to dog, those with a dog or cat in the home had higher Treg cell levels compared with those who did not. Among women sensitized to cat, those who had a dog or cat in the home had lower Treg cell levels compared with those who had no dog or cat. Gestational age at blood draw did not affect the associations. We conclude that Treg cell levels during pregnancy vary in association with both dog and cat exposure and atopic status.

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### **Biostatistics & Research Epidemiology**

Williams, G. C., H. Patrick, C. P. Niemiec, L. K. Williams, G. Divine, J. E. Lafata, M. Heisler, K. Tunceli and M. Pladevall (2009). "Reducing the Health Risks of Diabetes How Self-determination Theory May Help Improve Medication Adherence and Quality of Life." Diabetes Educator **35**(3): 484-492. [Article Request Form](#)

[Williams, Geoffrey C.] Univ Rochester, Dept Med, Rochester, NY 14627 USA. [Williams, Geoffrey C.; Divine, George; Lafata, Jennifer Elston; Tunceli, Kaan; Pladevall, Manel] Henry Ford Hosp, Detroit, MI 48202 USA. [Heisler, Michele] Ann Arbor Hlth Syst, Vet Affairs Ctr Clin Practice Management Res, Ann Arbor, MI USA. [Heisler, Michele] Univ Michigan, Dept Internal Med, Ann Arbor, MI 48109 USA. [Heisler, Michele] Ctr Diabet Res & Training, Ann Arbor, MI USA.

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**Purpose** The purpose of this study is to apply the self-determination theory (SDT) model of health behavior to predict medication adherence, quality of life, and physiological outcomes among patients with diabetes.  
**Methods** Patients with diabetes (N = 2973) receiving care from an integrated health care delivery system in 2003 and 2004 were identified from automated databases and invited to participate in this study. In 2005, patients responded to a mixed telephone-and-mail survey assessing perceived autonomy support from health

care providers, autonomous self-regulation for medication use, perceived competence for diabetes self-management, medication adherence, and quality of life. In 2006, pharmacy claims data were used to indicate medication adherence, and patients' non-high-density lipoprotein (HDL) cholesterol, A1C, and glucose levels were assessed. Results The SDT model of health behavior provided adequate fit to the data. As hypothesized, perceived autonomy support from health care providers related positively to autonomous self-regulation for medication use, which in turn related positively to perceived competence for diabetes self-management. Perceived competence then related positively to quality of life and medication adherence, and the latter construct related negatively to non-HDL cholesterol, A1C, and glucose levels. Conclusions Health care providers' support for patients' autonomy and competence around medication use and diabetes self-management related positively to medication adherence, quality of life, and physiological outcomes among patients with diabetes.

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### **Bone & Joint Center**

Hurbanek, J. G., K. Anderson, S. Crabtree and G. J. Karnes (2009). "Biomechanical comparison of the docking technique with and without humeral bioabsorbable interference screw fixation." Am J Sports Med **37**(3): 526-33. [PDF Full-Text](#)

Henry Ford Hospital, Detroit, Michigan, USA.

**BACKGROUND:** Surgical reconstruction of the ulnar collateral ligament has evolved since Frank Jobe's original description. The "docking technique" is a popular modification that allows for securing the graft within a single humeral tunnel. More recently, interference screw fixation has been introduced as a means of improving the ultimate strength, stiffness, and kinematics of these constructs. **PURPOSE:** This study was conducted to compare the biomechanical performance of the docking technique with and without interference screw fixation in the humerus. **STUDY DESIGN:** Controlled laboratory study. **METHODS:** Nine matched pairs of human cadaveric elbows (age 49.9 +/- 8.0 years) were reconstructed with a tendon graft using the docking technique (group 1) or the docking technique with the addition of a 4.75-mm bioabsorbable humeral interference screw (group 2). Before the reconstruction, joint laxity was measured on each specimen with the ulnar collateral ligament intact and then after transection of the ligament. Laxity measurements were repeated after the reconstruction. Failure testing was then performed at 70 degrees of elbow flexion. The specimens were preloaded with a 1-N.m moment and then loaded to failure at a displacement rate of 14 mm/s to approximate 50% strain per second. **RESULTS:** Within group 1, the elbow laxity of the reconstructed state was significantly greater than the intact state at all tested flexion angles ( $P < .021$ ). Within group 2, no statistically significant difference existed in elbow laxity between the intact state and the reconstructed state. When comparing laxities between groups, group 1 tended to be more lax at all tested flexion angles but was only significantly greater at 105 degrees of flexion. The most common mode of failure for both groups involved the sutures pulling out of the tendon. No significant difference was found for ultimate moment of failure between the 2 groups. However, the moment associated with 3 mm of gap formation for group 2 (12.8 +/- 4.2 N x m) was statistically greater than that of group 1 (7.5 +/- 1.2 N x m) ( $P = .001$ ). The stiffness of group 2 (14.7 +/- 6.4 N/mm) was significantly greater than group 1 (9.9 +/- 3.1 N/mm) ( $P = .044$ ). **CONCLUSION:** The biomechanical performance of the docking technique with and without a humeral interference screw is similar. **CLINICAL RELEVANCE:** The stiffness of the construct, along with the difference in moment that allows a 3-mm gap formation, suggests that the addition of a humeral interference screw is potentially beneficial. Further research in a healing model will help clarify this benefit.

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### **Bone & Joint Center**

Sterba, W., D. G. Kim, D. P. Fyhrie, Y. N. Yeni and R. Vaidya (2009). "Biomechanical analysis of differing pedicle screw insertion angles (vol 22, pg 385, 2007)." Clinical Biomechanics **24**(5): 465-465. [PDF Full-Text](#)

[Sterba, William; Kim, Do-Gyoon; Yeni, Yener N.; Vaidya, Rahul] Henry Ford Hosp, Dept Orthopaed Surg, Detroit, MI 48202 USA. [Fyhrie, David P.] Univ Calif Davis, Sch Med, Orthopaed Res Labs, Sacramento, CA 95817 USA.

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## **Bone & Joint Center**

Yeni, Y. N., X. N. Dong, B. Zhang, G. J. Gibson and D. P. Fyhrie (2009). "Cancellous Bone Properties and Matrix Content of TGF-beta2 and IGF-I in Human Tibia: A Pilot Study." Clin Orthop Relat Res **EPub Ahead of Print**. [Article Request Form](#)

Department of Orthopaedics and Rehabilitation, Section of Biomechanics, Bone and Joint Center, Henry Ford Hospital, 2799 West Grand Boulevard, E&R 2015, Detroit, MI, 48202, USA, [yeni@bjc.hfh.edu](mailto:yeni@bjc.hfh.edu).

Transforming and insulin-like growth factors are important in regulating bone mass. Thus, one would anticipate correlations between matrix concentrations of growth factors and functional properties of bone. We therefore investigated the relationships of (1) TGF-beta2 and (2) IGF-I matrix concentrations with the trabecular microstructure, stress distribution, and mechanical properties of tibial cancellous bone from six male human cadavers. Trabecular stress amplification (VMExp/sigma(app)) and variability (VMCOV) were calculated using microcomputed tomography (muCT)-based finite element simulations. Bone volume fraction (BV/TV), surface/volume ratio (BS/BV), trabecular thickness (Tb.Th), number (Tb.N) and separation (Tb.Sp), connectivity (Eu.N), and anisotropy (DA) were measured using 3-D morphometry. Bone stiffness and strength were measured by mechanical testing. Matrix concentrations of TGF-beta2 and IGF-I were measured by ELISA. We found higher matrix concentrations of TGF-beta2 were associated with higher Tb.Sp and VMExp/sigma(app) for pooled data and within subjects. Similarly, a higher matrix concentration of IGF-I was associated with lower stiffness, strength, BV/TV and Tb.Th and with higher BS/BV, Tb.Sp, VMExp/sigma(app) and VMCOV for pooled data and within subjects. IGF-I and Tb.N were negatively associated within subjects. It appears variations of the stress distribution in cancellous bone correlate with the variation of the concentrations of TGF-beta2 and IGF-I in bone matrix: increased local matrix concentrations of growth factors are associated with poor biomechanical and architectural properties of tibial cancellous bone.

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## **Cardiology**

Al-Mallah, M. H., H. Hatahet, J. L. Cavalcante and S. Khanal (2009). "Low admission LDL-cholesterol is associated with increased 3-year all-cause mortality in patients with non ST segment elevation myocardial infarction." Cardiology Journal **16(3)**: 227-233. [Article Request Form](#)

[Al-Mallah, Mouaz H.] Henry Ford Heart & Vasc Inst, Div Cardiol, Detroit, MI 48202 USA. Al-Mallah, MH, Henry Ford Heart & Vasc Inst, Div Cardiol, K14,2799 W Grand Blvd, Detroit, MI 48202 USA. [malmall1@hfhs.org](mailto:malmall1@hfhs.org)

Background: The relationship between admission low-density lipoprotein (LDL) levels and long-term outcomes has not been established in patients with acute coronary syndrome. We tested the hypothesis that patients who develop non-ST segment elevation myocardial infarction (NSTEMI) despite low LDL have a worse cardiovascular outcome in the long term. Methods: Patients admitted with NSTEMI between 1 January 1997 and 31 December 2000 and with fasting lipid profiles measured within 24 hours of admission were selected for analysis. Baseline characteristics and 3-year all-cause mortality were compared between the patients with LDL above and below the median. Multivariate analysis was used to determine the predictors of all-cause mortality, and adjusted survival was analyzed using the Cox proportional hazard model. Results: Of the total of 517 patients, 264 had LDL  $\leq$  105 mg/dL and 253 had LDL  $>$  105 mg/dL. There was no difference in age, gender, severity of coronary artery disease, and left ventricular ejection fraction between the 2 groups. Thirty-six percent of patients with LDL  $\leq$  105 mg/dL and 24% of patients with LDL  $>$  105 mg/dL were on lipid-lowering therapy on admission. After 3 years, patients with admission LDL  $\leq$  105 mg/dL had higher all-cause mortality rate compared to patients with LDL  $>$  105 mg/dL (14.8% vs. 7.1%,  $p = 0.005$ ). The higher all-cause mortality persisted (OR 1.8, 95% CI 1.0-3.5,  $p = 0.05$ ) even after adjustment for confounding variables. Conclusions: In our cohort, lower LDL-cholesterol at admission was associated with decreased 3-year survival in patients with NSTEMI. neither this was a result of current therapy or a marker for worse baseline characteristics needs to be studied further. (Cardiol J 2009; 16, 3: 227-233)

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## Cardiology

Collins, S. P., W. F. Peacock, C. J. Lindsell, P. Clopton, D. B. Diercks, B. Hiestand, C. Hogan, M. C. Kontos, C. Mueller, R. Nowak, W. J. Chen, C. H. Huang, W. T. Abraham, E. Amsterdam, T. Breidhardt, L. Daniels, A. Hasan, M. Hudson, J. McCord, T. Naz, L. E. Wagoner and A. Maisel (2009). "S3 Detection as a Diagnostic and Prognostic Aid in Emergency Department Patients With Acute Dyspnea." Annals of Emergency Medicine 53(6): 748-757. [PDF Full-Text](#)

[Collins, Sean P.; Lindsell, Christopher J.] Univ Cincinnati, Dept Emergency Med, Cincinnati, OH 45267 USA. [Naz, Tehmina] Univ Cincinnati, Dept Internal Med, Div Cardiol, Cincinnati, OH 45267 USA. [Peacock, W. Frank] Cleveland Clin Fdn, Dept Emergency Med, Cleveland, OH 44195 USA. [Clopton, Paul] San Diego VA Med Ctr, Res Serv, San Diego, CA USA. [Daniels, Lori; Maisel, Alan] San Diego VA Med Ctr, Div Cardiol, San Diego, CA USA. [Diercks, Deborah B.] Univ Calif Davis, Dept Emergency Med, Davis, CA 95616 USA. [Amsterdam, Ezra] Univ Calif Davis, Dept Internal Med, Div Cardiol, Davis, CA 95616 USA. [Hiestand, Brian] Ohio State Univ, Dept Emergency Med, Div Cardiol, Columbus, OH 43210 USA. [Abraham, William T.; Hasan, Ayesha] Ohio State Univ, Dept Internal Med, Div Cardiol, Columbus, OH 43210 USA. [Kontos, Michael C.] Virginia Commonwealth Univ, Dept Internal Med, Div Cardiol, Richmond, VA USA. [Mueller, Christian; Breidhardt, Tobias] Univ Basel, Dept Internal Med, Basel, Switzerland. [Hudson, Mike; McCord, James] Henry Ford Hlth Syst, Div Cardiol, Dept Emergency Med, Detroit, MI USA. [Chen, Wen-Jone] Natl Taiwan Univ Hosp, Dept Emergency Med, Taipei, Taiwan. [Huang, Chien-Hua] Natl Taiwan Univ Med Coll & Hosp, Dept Emergency Med, Taipei, Taiwan. [Wagoner, Lynne E.] Greater Cincinnati Cardiovasc Consultants, Cincinnati, OH USA. Collins, SP, Univ Cincinnati, Dept Emergency Med, 231 Albert Sabin Way, Cincinnati, OH 45267 USA. [sean.collins@uc.edu](mailto:sean.collins@uc.edu)

Study objective: Dyspneic emergency department (ED) patients present a diagnostic dilemma. Recent technologic advances have made it possible to capture information about pathologic heart sounds at ECG recording. This study evaluates the effect of an S3 captured by acoustic cardiography on emergency physician diagnostic accuracy and confidence in their diagnosis of acute decompensated heart failure, as well as the patient's prognosis. Methods: Dyspneic ED patients older than 40 years who were not dialysis dependent were prospectively enrolled in this multinational study. Treating emergency physicians, initially blinded to all laboratory and acoustic cardiography results, estimated acute decompensated heart failure probability from 0% to 100% on a visual analog scale. The emergency physician repeated the visual analog scale after acoustic cardiography results were provided. Physician diagnostic accuracy for and confidence in acute decompensated heart failure were evaluated against a reference standard diagnosis, as determined by 2 independent cardiologists blinded to acoustic cardiography. Patients were followed through 90 days to determine the relationship of the S3 to adverse events. Results: Nine hundred ninety-five patients with acoustic cardiography results were enrolled from March to October 2006 at 7 US and 2 international sites. Median age was 63 years, 55% were men, and 44% were white. The reference diagnosis was acute decompensated heart failure in 41.5%. After initial history and physical examination, the treating physician's initial sensitivity, specificity, and accuracy for acute decompensated heart failure as a possible diagnosis were 89.0% (95% confidence interval [CI] 85.5% to 91.8%), 58.2% (95% CI 54.0% to 62.2%), and 71.0% (95% CI 68.4% to 73.8%), respectively. Acoustic cardiography had an accuracy of 68% (95% CI 65.4% to 71.3%), sensitivity of 40.2% (95% CI 35.5% to 45.1%), and specificity of 88.5% (95% CI 85.5% to 90.9%). Emergency physician confidence and diagnostic accuracy were influenced by adding information about the presence or absence of S3. In a multivariable model, the S3 added no independent prognostic information for 30-day (odds ratio 1.20; 95% CI 0.67 to 2.14) or 90-day events (odds ratio 1.22; 95% CI 0.78 to 1.90). Conclusion: In patients presenting with acute dyspnea, the acoustic cardiography S3 was specific for acute decompensated heart failure and affected physician confidence but did not improve diagnostic accuracy for acute decompensated heart failure, largely because of its low sensitivity. Further, the acoustic cardiography S3 provided no significant independent prognostic information. [Ann Emerg Med. 2009;53:748-757.]

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## Cardiology

Colombo, P. C., S. Rastogi, D. Onat, V. Zaca, R. C. Gupta, U. P. Jorde and H. N. Sabbah (2009). "Activation of Endothelial Cells in Conduit Veins of Dogs With Heart Failure and Veins of Normal Dogs After Vascular Stretch by Acute Volume Loading." Journal of Cardiac Failure **15**(5): 457-463. [PDF Full-Text](#)

[Rastogi, Sharad; Zaca, Valerio; Gupta, Ramesh C.; Sabbah, Hani N.] Henry Ford Hosp, Dept Med, Div Cardiovasc Med, Detroit, MI 48202 USA. [Colombo, Paolo C.; Onat, Duygu; Jorde, Ulrich P.] Columbia Univ, Dept Med, Div Cardiol, New York Presbyterian Hosp, Coll Phys & Surg, New York, NY USA.

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Background: The venous endothelium is a key regulator of central blood volume, organ perfusion, and hemostasis in heart failure (HF). We previously reported activation of the inflammatory/oxidative program in venous endothelial cells collected from decompensated HF patients. The underlying Causes are unknown. We tested the hypothesis that the pro-inflammatory state of HF and vascular strain associated with congestion can activate the endothelial inflammatory/oxidative and hemostatic programs. Methods and Results: We studied 6 normal (NL) dogs (left ventricular ejection fraction [LVEF] >50%, central venous pressure [CVP] = 8 +/- 2 mm Hg) and 6 dogs with HF (LVEF similar to 30%, CVP 8 +/- 2 mm Hg) produced by intracoronary microembolizations. Normal clogs were studied at baseline and 1 hour after fluid load to it target CVP >= 20 mm Hg. Endothelial cells were scraped from jugular veins mRNA expression was analyzed by reverse transcription polymerase chain reaction. The endothelial inflammatory/oxidative and hemostatic programs were significantly activated in HF clogs compared with NL. In NL clogs, fluid load significantly activated the endothelial inflammatory/oxidative and hemostatic programs, and, concurrently, caused a significant increase in plasma neurohumoral indices to levels that approached those of HF dogs. Conclusions: The pro-inflammatory state of HF and vascular strain associated with congestion can both activate venous endothelial cells in dogs in a manner consistent with that seen in HF patients. (J Cardiac Fail 2009;15:457-403)

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## Cardiology

Gheorghiade, M., K. F. Adams, J. G. F. Cleland, G. Cotter, G. M. Felker, G. S. Filippatos, G. C. Fonarow, B. H. Greenberg, A. F. Hernandez, S. Khan, M. Komajda, M. A. Konstam, P. P. Liu, A. P. Maggioni, B. M. Massie, J. J. McMurray, M. Mehra, M. Metra, J. O'Connell, C. M. O'Connor, P. S. Pang, I. L. Pina, H. N. Sabbah, J. R. Teerlink, J. E. Udelson, C. W. Yancy, F. Zannad and N. Stockbridge (2009). "Phase III clinical trial end points in acute heart failure syndromes: A virtual roundtable with the acute heart failure syndromes international working group." American Heart Journal **157**(6): 957-970. [PDF Full-Text](#)

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### Cardiology

Shah, S. J., J. E. A. Blair, G. S. Filippatos, C. Macarie, W. Ruzylo, J. Korewicki, S. I. Bubenek-Turconi, M. Ceracchi, M. Bianchetti, P. Carminati, D. Kremastinos, J. Grzybowski, G. Valentini, H. N. Sabbah and M. Gheorghiade (2009). "Effects of istaroxime on diastolic stiffness in acute heart failure syndromes: Results from the Hemodynamic, Echocardiographic, and Neurohormonal Effects of Istaroxime, a Novel Intravenous Inotropic and Lusitropic Agent: a Randomized Controlled Trial in Patients Hospitalized with Heart Failure (HORIZON-HF) trial." *American Heart Journal* **157**(6): 1035-1041. [PDF Full-Text](#)

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Background Istaroxime is a novel intravenous agent with inotropic and lusitropic properties related to inhibition of the Na<sup>+</sup>/K<sup>+</sup> adenosine triphosphatase and stimulation of sarcoplasmic reticulum calcium adenosine triphosphatase activity. We analyzed data from HORIZON-HF, a randomized, controlled trial evaluating the short-term effects of istaroxime in patients hospitalized with heart failure and left ventricular ejection fraction : <= 35% to test the hypothesis that istaroxime improves diastolic stiffness in acute heart failure syndrome. Methods One hundred twenty patients were randomized 3:1 (istaroxime/placebo) to a continuous 6-hour infusion of 1 of 3 doses of istaroxime or placebo. All patients underwent pulmonary artery catheterization and comprehensive 2-dimensional/Doppler and tissue Doppler echocardiography at baseline and at the end of the 6-hour infusion. We quantified diastolic stiffness using pressure-volume analysis and tissue Doppler imaging of the lateral mitral annulus (E'). Results Baseline characteristics were similar among all groups, with mean age 55 +/- 11 years, 88% men, left ventricular ejection fraction 27% +/- 7%, systolic blood pressure (SBP) 116 +/- 13 mm Hg, and pulmonary capillary wedge pressure (PCWP) 25 +/- 5 mm Hg. Istaroxime administration resulted in an increase in E' velocities, whereas there was a decrease in E' in the placebo group (P = .048 between groups). On pressure-volume analysis, istaroxime decreased end-diastolic elastance (P = .0001). On multivariate analysis, increasing doses of istaroxime increased E' velocity (P = .043) and E-wave deceleration time (P = .001), and decreased E/E' ratio (P = .047), after controlling for age, sex, baseline ejection fraction, change in PCWP, and change in SBP. Conclusions Istaroxime decreases PCWP, increases SBP, and decreases diastolic stiffness in patients with acute heart failure syndrome. (Am Heart J 2009;157:1035-41.)

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### Cardiology

Sinno, M. C., M. Kowalski, D. N. Kenigsberg, S. Khanal and S. C. Krishnan (2009). "Intracoronary electrocardiographic deflections during transmural ischemia induced by percutaneous transluminal coronary angioplasty." *J Electrocardiol* **EPub Ahead of Print**. [Article Request Form](#)

Henry Ford Hospital, Detroit, MI, USA.

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## Cardiology

Valdez-Lowe, C., S. A. Ghareeb and N. T. Artinian (2009). "Pulse oximetry in adults." Am J Nurs **109**(6): 52-9; quiz 60. [PDF Full-Text](#)

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Pulse oximetry, a straightforward method for estimating arterial oxygen saturation, can detect hypoxemia early; it's used often and in a variety of settings. But what's not always clear is how frequently-or even whether-patients should be monitored, and unless guidelines are understood and followed, pulse oximetry can be misused or overused. This article reviews the technology and its limitations and discusses current guidelines and their implications for nurses.

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## Cardiology

Zaca, V., S. Rastogi, S. Mishra, M. Wang, V. G. Sharov, R. C. Gupta, S. Goldstein and H. N. Sabbah (2009). "Atenolol is inferior to metoprolol in improving left ventricular function and preventing ventricular remodeling in dogs with heart failure." Cardiology **112**(4): 294-302.  
[Article Request Form](#)

Department of Medicine, Division of Cardiovascular Medicine, Henry Ford Heart and Vascular Institute, Detroit, MI 48202, USA.

OBJECTIVES: beta-Blockers are standard therapy for patients with heart failure (HF). This study compared the effects of chronic monotherapy with 2 different beta(1)-selective adrenoceptor blockers, namely atenolol and metoprolol succinate, on left ventricular (LV) function and remodeling in dogs with coronary microembolization-induced HF [LV ejection fraction (EF) 30-40%]. METHODS: Twenty HF dogs were randomized to 3 months of therapy with atenolol (50 mg once daily, n = 6), metoprolol succinate (100 mg, once daily, n = 7) or to no therapy (control, n = 7). LV EF and volumes were measured before initiating therapy and after 3 months of therapy. The change (Delta) in EF and volumes between measurements before and after therapy was calculated and compared among study groups. RESULTS: In controls, EF decreased and end-systolic volume increased. Atenolol prevented the decrease in EF and the increase in ESV. In contrast, metoprolol succinate significantly increased EF and decreased end-systolic volume. DeltaEF was significantly higher and Deltaend-systolic volume significantly lower in metoprolol succinate-treated dogs compared to atenolol-treated dogs (EF: 6.0 +/- 0.86% vs. 0.8 +/- 0.85%, p < 0.05; end-systolic volume: -4.3 +/- 0.81 ml vs. -1 +/- 0.52 ml, p < 0.05). CONCLUSIONS: In HF dogs, chronic therapy with atenolol does not elicit the same LV function and remodeling benefits as those achieved with metoprolol succinate.

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## Cardiology

Zheng, S. K., Y. Xia, A. Bidthanapally, F. Badar, I. Ilsar and N. Duvoisin (2009). "Damages to the extracellular matrix in articular cartilage due to cryopreservation by microscopic magnetic resonance imaging and biochemistry." Magnetic Resonance Imaging **27**(5): 648-655. [PDF Full-Text](#)

[Zheng, ShaoKuan; Xia, Yang; Bidthanapally, Aruna; Badar, Farid; Duvoisin, Nick] Oakland Univ, Dept Phys, Rochester, MI 48309 USA. [Zheng, ShaoKuan; Xia, Yang; Bidthanapally, Aruna; Badar, Farid; Duvoisin, Nick] Oakland Univ, Ctr Biomed Res, Rochester, MI 48309 USA. [Ilsar, Itamar] Henry Ford Hlth Syst, Inst Heart & Vasc, Detroit, MI 48202 USA. Xia, Y, Oakland Univ, Dept Phys, Rochester, MI 48309 USA. [xia@oakland.edu](mailto:xia@oakland.edu)

To investigate the damages to the extracellular matrix in articular cartilage due to cryopreservation, the depth-dependent concentration profiles of glycosaminoglycans (GAGs) in 34 cartilage specimens from canine

humeral heads were imaged at 13- $\mu$ m pixel resolution using the in vitro version of the dGEMRIC protocol in microscopic MRI ( $\mu$  MRI). In addition, a biochemical assay was used to determine the GAG loss from the tissue to the solution where the tissue was immersed. For specimens that had been frozen at -20 degrees C or -80 degrees C without any cryoprotectant, a significant loss of GAG (as high as 56.5%) was found in cartilage, dependent upon the structural zones of the tissue and the conditions of cryopreservation. The cryoprotective abilities of dimethyl sulfoxide (DMSO) as a function of its concentration in saline and storage temperature were also investigated. A 30% DMSO concentration was sufficient in preventing the reduction of GAG in the tissue at the -20 degrees C storage temperature, but a 50% concentration of DMSO was necessary for the -80 degrees C cryopreservation. These imaging results were verified by the biochemical analysis.

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### **Center for Health Services Research**

Lafata, J., O. Tunceli, M. Cerghet, K. Sharma and R. Lipton (2009). "The use of migraine preventive medications among patients with and without migraine headaches." Cephalalgia. **Epub Ahead of Print.** [Article Request Form](#)

Center for Health Services Research, Henry Ford Hospital, Detroit, USA.

The aim was to describe the use of and adherence to migraine preventives among insured patients meeting the International Classification of Headache Disorders, 2nd edn (ICHD-II) criteria for migraine headaches. A retrospective, case-control study was conducted using data from a telephone interview linked with health insurance claims data. Subjects were health plan enrollees aged 18-55 years who had incurred at least one encounter between June 2000 and November 2001. Interview responses were used to identify cases meeting the ICHD-II criteria for strict and probable migraine and a random sample of controls. Pharmacy claims data were used to construct measures of use and adherence. Differences in outcomes by adherence status were evaluated using generalized linear models. We identified 2517 cases and 941 controls. Among cases, the prevalence of antidepressant use was 4%, anticonvulsant use was 1.9%, antihypertensive use was 8.9%. Combined use was 13.4% among cases and did not differ significantly from that observed among controls (12.4%). Mean adherence rate between the first and last dispensing during the year was high (88%) and did not differ by migraine status. When the entire 12-month period is considered, adherence was substantially lower (56%). Patients who were adherent between dispensings reported significantly less migraine-related disability and incurred higher prescription drug costs, but did not differ in their total medical care costs. Patients with migraine are unlikely to be users of preventive medications. Among users, few are taking preventive medications continuously. Patients with migraine-especially those without a medical diagnosis for migraine or headaches-are not receiving the benefits available from existing pharmacotherapy options.

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### **Center for Health Services Research**

Tunceli, K., P. F. Short, J. R. Moran and O. Tunceli (2009). "Cancer survivorship, health insurance, and employment transitions among older workers." Inquiry **46**(1): 17-32. [Article Request Form](#)

Center for Health Services Research, Henry Ford Health Systems, USA.

This study examined the effect of job-related health insurance on employment transitions (labor force exits, reductions in hours, and job changes) of older working cancer survivors. Using multivariate models, we compared longitudinal data for the period 1997-2002 from the Penn State Cancer Survivor Study to similar data for workers with no cancer history in the Health and Retirement Study, who were also ages 55 to 64 at follow-up. The interaction of cancer survivorship with health insurance at diagnosis was negative and significant in predicting labor force exits, job changes, and transitions to part-time employment for both genders. The differential effect of job-related health insurance on the labor market dynamics of cancer survivors represents an additional component of the economic and psychosocial burden of cancer on survivors.

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### **Dermatology**

Chong, B. F. and H. K. Wong (2009). "Treatment of psoriasis with etanercept in a patient with a history of primary B-cell lymphoma." Clinical and Experimental Dermatology **34**(5): E11-E13. [PDF Full-Text](#)

[Chong, B. F.; Wong, H. K.] Henry Ford Hosp, Dept Dermatol, Detroit, MI 48202 USA.  
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The use of immunobiologicals that suppress an overly active immune system in psoriasis carries with it the possibility of cancer development as a result of immunosuppression. Patients with a history of malignancy may be at risk for recurrence when treated with immunosuppressive agents. Moreover, autoimmune diseases, such as psoriasis, have been associated with an increased risk of lymphoma. Therefore, risk-benefit assessments must take into account the clinical severity and treatment of psoriasis. We describe a 59-year-old white man with a history of primary B-cell lymphoma, severe recalcitrant plaque-type psoriasis and psoriatic arthritis, who was started on etanercept for treatment of his psoriasis and psoriatic arthritis. The patient has a long history of remission of his lymphoma. After treatment, the patient experienced significant global improvement with essentially complete remission of the cutaneous lesions and arthritis, and had no recurrence of his lymphoma or other systemic complications while on etanercept after follow-up for > 3 years.

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### **Dermatology**

Criscione, V. D., M. A. Weinstock, M. F. Naylor, C. Luque, M. J. Eide and S. F. Bingham (2009). "Actinic Keratoses Natural History and Risk of Malignant Transformation in the Veterans Affairs Topical Tretinoin Chemoprevention Trial." Cancer **115**(11): 2523-2530.

[PDF Full-Text](#)

[Criscione, Vincent D.; Weinstock, Martin A.; Luque, Claudia] Vet Adm Med Ctr, Dermatoepidemiol Unit, Providence, RI 02908 USA. [Criscione, Vincent D.; Weinstock, Martin A.] Brown Univ, Dept Dermatol, Providence, RI 02912 USA. [Criscione, Vincent D.; Weinstock, Martin A.] Brown Univ, Dept Community Hlth, Providence, RI 02912 USA. [Weinstock, Martin A.] Rhode Isl Hosp, Dept Dermatol, Providence, RI USA. [Naylor, Mark F.] Vet Affairs Med Ctr, Dept Dermatol, Oklahoma City, OK 73104 USA. [Eide, Melody J.] Henry Ford Hosp, Dept Dermatol, Detroit, MI 48202 USA. [Bingham, Stephen F.] Vet Affairs Cooperat Studies Coordinating Ctr, Perry Point, MD USA.  
Weinstock, MA, Vet Adm Med Ctr, Dermatoepidemiol Unit 111D, 830 Chalkstone Ave, Providence, RI 02908 USA. [maw@brown.edu](mailto:maw@brown.edu)

BACKGROUND: Actinic keratoses (AKs) are established as direct precursors of squamous cell carcinoma (SCC), but there is significant controversy regarding the rate at which AKs progress to SCC. The authors of this report studied a high-risk population to estimate the risk of progression of AK to SCC and to basal cell carcinoma (BCC) and the risk of spontaneous regression of untreated AKs. METHODS: Data were obtained from participants in the Department of Veterans Affairs Topical Tretinoin Chemoprevention Trial. Participants were examined every 6 months for up to 6 years. At each examination, the locations on the face and ears of clinically diagnosed AKs and lesions scheduled for biopsy were marked, and high-resolution digital photographs were taken. These photographs were used later to map and track the presence, absence, or biopsy of each AK across visits. RESULTS: In total, 7784 AKs were identified on the face and ears of 169 participants. The risk of progression of AK to primary SCC (invasive or in situ) was 0.60% at 1 year and 2.57% at 4 years. Approximately 65% of all primary SCCs and 36% of all primary BCCs diagnosed in the study cohort arose in lesions that previously were diagnosed clinically as AKs. The majority of AKs (55%) that were followed clinically were not present at the 1-year follow-up, and the majority (70%) were not present at the 5-year follow-up. CONCLUSIONS: In the current study, the authors quantified the malignant potential of clinically diagnosed AKs for both SCC and BCC, although many did not persist, and the results suggested that AKs may play a greater role in the overall burden of keratinocyte carcinomas than previously documented.

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### **Dermatology**

Hexsel, C. L., M. J. Eide, C. C. Johnson, R. Krajenta, G. Jacobsen, I. Hamzavi and H. W. Lim (2009). "Incidence of nonmelanoma skin cancer in a cohort of patients with vitiligo." J Am Acad Dermatol **60**(6): 929-33. [PDF Full-Text](#)

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

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

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### **Dermatology**

Srivastava, D. and D. J. Kouba (2009). "A "Lilliputian" Technique for Rapid and Efficient Securing of Bolster Dressings Over Full-Thickness Skin Grafts." Dermatol Surg **Epub Ahead of Print**. [PDF Full-Text](#)

Department of Dermatology of the Henry Ford Medical Center, Detroit, Michigan.

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### **Dermatology**

Wakade, O., B. Adams and T. Shwayder (2009). "Acral Peeling Skin Syndrome: A Case of Two Brothers." Pediatric Dermatology **26**(3): 328-330. [PDF Full-Text](#)

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Adams, B, Henry Ford Hosp, Dept Dermatol, 3031 W Grand Blvd, Detroit, MI 48202 USA.  
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We report two brothers of Middle Eastern descent with consanguineous parents who present with numerous fragile, flaccid blisters on the hands and feet. In addition to spontaneous peeling, they can manually peel skin from acral areas without pain. The symptoms worsen with warm temperatures, excessive water exposure, and perspiration. Two biopsies from flaccid blisters on the feet were taken from the older brother, which revealed cleavage at the level of the stratum corneum. A diagnosis of acral peeling skin syndrome was made.

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### **Dermatology**

Zhou, L., K. H. Seo, H. Z. He, R. Pacholczyk, D. M. Meng, C. G. Li, J. Xu, J. X. She, Z. Dong and Q. S. Mi (2009). "Tie2cre-induced inactivation of the miRNA-processing enzyme Dicer disrupts invariant NKT cell development." Proc Natl Acad Sci U S A **106**(25): 10266-71. PMC2700920. [PDF Full-Text](#)

Henry Ford Immunology Program, and Department of Dermatology, Henry Ford Hospital, Detroit, MI 48202, USA.

MicroRNAs (miRNAs) are a class of evolutionarily conserved small noncoding RNAs that are increasingly being recognized as important regulators of gene expression. The ribonuclease III enzyme Dicer is essential for the processing of miRNAs. CD1d-restricted invariant natural killer T (iNKT) cells are potent regulators of diverse immune responses. The role of Dicer-generated miRNAs in the development and function of immune regulatory iNKT cells is unknown. Here, we generated a mouse strain with a tissue-specific disruption of Dicer, and showed that lack of miRNAs after the deletion of Dicer by Tie2-Cre (expressed in hematopoietic cells and endothelial cells) interrupted the development and maturation of iNKT cells in the thymus and significantly decreased the number of iNKT cells in different immune organs. Thymic and peripheral iNKT cell compartments were changed in miRNA-deficient mice, with a significantly increased frequency of CD4(+)CD8(+) iNKT cells in the thymus and a significantly decreased frequency of CD4(+) iNKT cells in the spleen. MiRNA-deficient iNKT cells display profound defects in alpha-GalCer-induced activation and cytokine production. Bone marrow (BM) from miRNA-deficient mice poorly reconstituted iNKT cells compared to BM from WT mice. Also, using a thymic iNKT cell transfer model, we found that iNKT cell homeostasis was impaired in miRNA-deficient recipient mice. Our data indicate that miRNAs expressed in hematopoietic cells and endothelial cells are potent regulators of iNKT cell development, function, and homeostasis.

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## **Dermatology**

Zhou, L., K. H. Seo, H. K. Wong and Q. S. Mi (2009). "MicroRNAs and immune regulatory T cells." *Int Immunopharmacol* **9**(5): 524-7. [Article Request Form](#)

Henry Ford Hospital Immunology Program, Henry Ford Hospital, Detroit, MI, USA.

MicroRNAs (miRNAs)-mediated RNA interference are emerging as an important regulatory pathway for various biological processes, including development, differentiation, and homeostasis. Accumulated evidence suggests that miRNAs regulate T cell and B cell differentiation, proliferation, and apoptosis. Deletion of miRNAs in hematopoietic stem cells or in thymus disrupts T cell homeostasis and results in autoimmunity and abnormal cytokine production. Regulatory T cells are potent immune regulators. In this mini-review, we provide a brief overview of the important roles of miRNAs in the development and function of T cells, especially in immune regulatory T cells.

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## **Diagnostic Radiology**

Ali, M. M., G. Liu, T. Shah, C. A. Flask and M. D. Pagel (2009). "Using Two Chemical Exchange Saturation Transfer Magnetic Resonance Imaging Contrast Agents for Molecular Imaging Studies." *Acc Chem Res* **Epub Ahead of Print**. [PDF Full-Text](#)

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

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

CEST agents in an in vivo MRI study of a mouse model of mammary carcinoma. The ratio of the concentrations of the two CEST agents was quantified with analysis methods that parallel Michaelis-Menten enzyme kinetic analysis. This example demonstrates current limitations of the method that require additional research, but it also shows that two CEST MRI contrast agents can be detected and quantitatively assessed during in vivo molecular imaging studies.

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### **Diagnostic Radiology**

Janic, B., A. M. Rad, E. K. Jordan, A. S. Iskander, M. M. Ali, N. R. Varma, J. A. Frank and A. S. Arbab (2009). "Optimization and validation of FePro cell labeling method." PLoS One **4**(6): e5873. PMC2690694. [PDF Full-Text](#)

Cellular and Molecular Imaging Laboratory, Department of Radiology, Henry Ford Hospital, Detroit, MI, USA. [bjanic@rad.hfh.edu](mailto:bjanic@rad.hfh.edu)

Current method to magnetically label cells using ferumoxides (Fe)-protamine (Pro) sulfate (FePro) is based on generating FePro complexes in a serum free media that are then incubated overnight with cells for the efficient labeling. However, this labeling technique requires long (>12-16 hours) incubation time and uses relatively high dose of Pro (5-6 microg/ml) that makes large extracellular FePro complexes. These complexes can be difficult to clean with simple cell washes and may create low signal intensity on T2\* weighted MRI that is not desirable. The purpose of this study was to revise the current labeling method by using low dose of Pro and adding Fe and Pro directly to the cells before generating any FePro complexes. Human tumor glioma (U251) and human monocytic leukemia cell (THP-1) lines were used as model systems for attached and suspension cell types, respectively and dose dependent (Fe 25 to 100 microg/ml and Pro 0.75 to 3 microg/ml) and time dependent (2 to 48 h) labeling experiments were performed. Labeling efficiency and cell viability of these cells were assessed. Prussian blue staining revealed that more than 95% of cells were labeled. Intracellular iron concentration in U251 cells reached approximately 30-35 pg-iron/cell at 24 h when labeled with 100 microg/ml of Fe and 3 microg/ml of Pro. However, comparable labeling was observed after 4 h across the described FePro concentrations. Similarly, THP-1 cells achieved approximately 10 pg-iron/cell at 48 h when labeled with 100 microg/ml of Fe and 3 microg/ml of Pro. Again, comparable labeling was observed after 4 h for the described FePro concentrations. FePro labeling did not significantly affect cell viability. There was almost no extracellular FePro complexes observed after simple cell washes. To validate and to determine the effectiveness of the revised technique, human T-cells, human hematopoietic stem cells (hHSC), human bone marrow stromal cells (hMSC) and mouse neuronal stem cells (mNSC C17.2) were labeled. Labeling for 4 hours using 100 microg/ml of Fe and 3 microg/ml of Pro resulted in very efficient labeling of these cells, without impairing their viability and functional capability. The new technique with short incubation time using 100 microg/ml of Fe and 3 microg/ml of Pro is effective in labeling cells for cellular MRI.

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### **Diagnostic Radiology**

Kinni, V., J. Craig, M. van Holsbeeck and D. Ditmars (2009). "Entrapment of the posterior interosseous nerve at the arcade of Frohse with sonographic, magnetic resonance imaging, and intraoperative confirmation." J Ultrasound Med **28**(6): 807-12. [PDF Full-Text](#)

Wayne State University School of Medicine, Department of Radiology, Henry Ford Hospital, 2799 W Grand Blvd, Detroit, MI 48202, USA. [vkinni@med.wayne.edu](mailto:vkinni@med.wayne.edu)

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### **Diagnostic Radiology**

Wang, X. and S. Koch (2009). "Positron emission tomography/computed tomography potential pitfalls and artifacts." Curr Probl Diagn Radiol **38**(4): 156-69. [Article Request Form](#)

Department of Radiology, Henry Ford Health System, Detroit, MI 48202-2689, USA.

With the recent use of 18-fluoro-2-deoxyglucose (FDG) positron emission tomography (PET) for tumor staging and treatment response, it is important to recognize many pitfalls, artifacts, and benign uptakes that are

commonly encountered. Normal physiology can explain many regions of increased FDG activity, as well as incidental benign tumors and benign metabolic conditions. Recognition of characterization of benign causes and physiologic variants for FDG uptake are discussed to avoid improper characterization as a malignancy. A basic understanding of PET/computed tomographic physics is also discussed, in relation to attenuation correction artifacts caused by metallic implants and contrast agents in the gastrointestinal tract, as well as artifacts caused in fused images due to patient motion. Also presented is the rationale for expected, benign uptake in various metabolic diseases, as well as pharmacologic methods for decreasing the artifacts caused by metabolic diseases. PET/computed tomographic evaluation of the thyroid, thymus, adrenal adenomas, uterus and ovaries, infection/inflammatory changes, and postradiation/chemotherapy changes are also discussed, with expected normal changes, as well as pitfalls and artifacts.

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### **Emergency Medicine**

Nowak, M. R., A. W. Kirkpatrick, J. A. Bouffard, D. Amponsah and S. A. Dulchavsky (2009). "Snowboarding injuries: a review of the literature and an analysis of the potential use of portable ultrasound for mountainside diagnostics." *Curr Rev Musculoskelet Med* **2**(1): 25-9. PMC2684950. [PDF Full-Text](#)

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Snowboarding has become a popular recreational and professional sport. Participants suffer a variety of injuries, especially of the extremities, that require medical evaluation. This article reviews the reported injuries to both leisure and elite athletes. To many, an injured extremity requires travel to a medical facility for accurate evaluation. Musculoskeletal ultrasound is an accurate and portable technology that can be used for real time, mountainside diagnoses of these injuries.

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### **Emergency Medicine**

Suzuki, T., A. Distante, A. Zizza, S. Trimarchi, M. Villani, J. A. S. Uriarte, L. Schinosa, A. Renzulli, F. Sabino, R. Nowak, R. Birkhahn, J. E. Hollander, F. Counselman, R. Vijayendran, E. Bossone and K. Eagle (2009). "Diagnosis of Acute Aortic Dissection by D-Dimer The International Registry of Acute Aortic Dissection Substudy on Biomarkers (IRAD-Bio) Experience." *Circulation* **119**(20): 2702-7. [PDF Full-Text](#)

[Suzuki, Toru] Univ Tokyo, Grad Sch Med, Dept Cardiovasc Med, Bunkyo Ku, Tokyo 1138655, Japan. [Distante, Alessandro] Ist Sci Biomed Euro Mediterraneo, Brindisi, Italy. [Distante, Alessandro; Zizza, Antonella] CNR, Inst Clin Physiol, Lecce, Italy. [Distante, Alessandro] Univ Pisa, Sch Med, I-56100 Pisa, Italy. [Trimarchi, Santi] IRCCS Policlin San Donato, Milan, Italy. [Villani, Massimo] Vito Fazzi Hosp, Lecce, Italy. [Uriarte, Jorge Antonio Salerno] Univ Insubria, Osped Circolo, Varese, Italy. [Uriarte, Jorge Antonio Salerno] Fdn Macchi, Varese, Italy. [Schinosa, Luigi De Luca Tupputi] Policlin Hosp, Bari, Italy. [Renzulli, Attilio] UMG, Catanzaro, Italy. [Sabino, Federico] ALIV Healthcare R&D, Forte Dei Marmi, Italy. [Nowak, Richard] Henry Ford Hosp, Detroit, MI 48202 USA. [Birkhahn, Robert] New York Methodist Hosp, Brooklyn, NY USA. [Hollander, Judd E.] Univ Penn, Philadelphia, PA 19104 USA. [Counselman, Francis] Eastern Virginia Med Sch, Norfolk, VA 23501 USA. [Vijayendran, Ravi] Biosite, San Diego, CA USA. [Eagle, Kim] Univ Michigan, Ann Arbor, MI 48109 USA.

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Background-D-dimer has been reported to be elevated in acute aortic dissection. Potential use as a "rule-out" marker has been suggested, but concerns remain given that it is elevated in other acute chest diseases, including pulmonary embolism and ischemic heart disease. We evaluated the diagnostic performance of D-dimer testing in a study population of patients with suspected aortic dissection. Methods and Results-In this

prospective multicenter study, 220 patients with initial suspicion of having acute aortic dissection were enrolled, of whom 87 were diagnosed with acute aortic dissection and 133 with other final diagnoses, including myocardial infarction, angina, pulmonary embolism, and other uncertain diagnoses. D-dimer was markedly elevated in patients with acute aortic dissection. Analysis according to control disease, type of dissection, and time course showed that the widely used cutoff level of 500 ng/mL for ruling out pulmonary embolism also can reliably rule out aortic dissection, with a negative likelihood ratio of 0.07 throughout the first 24 hours. Conclusion-D-dimer levels may be useful in risk stratifying patients with suspected aortic dissection to rule out aortic dissection if used within the first 24 hours after symptom onset. (Circulation. 2009; 119: 2702-2707.)

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### **Endocrinology & Metabolism**

Al-Shoha, A., S. Qiu, S. Palnitkar and D. S. Rao (2009). "Osteomalacia with Bone Marrow Fibrosis Due to Severe Vitamin D Depletion Following Gastrointestinal Bypass Surgery for Severe Obesity." Endocr Pract **EPub Ahead of Print**: 1-16. [PDF Full-Text](#)

Bone & Mineral Research Laboratory, Henry Ford Hospital, 2799 W. Grand Blvd, Detroit, MI, USA.

**Objective:** To present 5 cases of bone biopsy proven osteomalacia with marrow fibrosis after gastric bypass surgery, review the relevant literature, and offer preventive strategies. **Methods:** We summarize the clinical presentation, relevant biochemical and radiological findings, and bone histomorphometry in 5 patients who developed severe vitamin D depletion following gastrointestinal bypass surgery for severe obesity seen over a period of 17 years. **Results:** Five patients (age 39-60y) were seen for evaluation of metabolic bone disease not responding to "usual" therapy following gastric bypass surgery. All had generalized bone pain and tenderness, muscle weakness, stooping posture, difficulty walking, and waddling gait due to severe proximal muscle weakness for a period of 2 to 5 years. Diagnoses before the referral varied from arthritis and gout to vitamin D deficiency and osteoporosis despite highly suggestive biochemical and/or radiological findings of osteomalacia in each patient, which was confirmed by bone biopsy. Following therapy with pharmacologic doses of ergocalciferol 100,000 IU daily and calcium carbonate 1 to 2.5 g/day there was a significant improvement in clinical symptoms and functional status, biochemical indices, bone mineral density and bone histomorphometry. **Conclusion:** Gastric bypass surgery predispose to severe vitamin D deficiency and osteomalacia in the absence of pharmacologic doses of vitamin D therapy. The current "usual" recommendations are grossly inadequate in this high risk population, and the clinical presentation is both non-specific and often misleading. Prospective long-term studies are needed to determine the appropriate vitamin D dose required to prevent osteomalacia in such patients.

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### **Endocrinology & Metabolism**

Sundaram, K., J. Senn, S. Yuvaraj, D. S. Rao and S. V. Reddy (2009). "FGF-2 Stimulation of RANK Ligand Expression in Paget's Disease of Bone." Mol Endocrinol **EPub Ahead of Print**. [Article Request Form](#)

Charles P. Darby Children's Research Institute, Medical University of South Carolina, Charleston, SC; Bristol Myers Squibb Pharmaceuticals, Syracuse, NY; Henry Ford Hospital, Detroit, Michigan.

RANK ligand (RANKL), a critical osteoclastogenic factor expressed in marrow stromal/preosteoblast cells is upregulated in Paget's disease of bone (PDB). We previously demonstrated that heat shock factor-2 (HSF-2) is a downstream target of fibroblast growth factor-2 (FGF-2) signaling to induce RANKL expression in bone marrow stromal/preosteoblast cells. In this study, we identified a 2.5-fold increase in serum FGF-2 levels in patients (n=8) with PDB compared to normal subjects (n=10). We showed that HSF-2 co-immunoprecipitates with heat shock protein-27 (HSP-27) and that FGF-2 stimulation significantly increased phospho-HSP-27 levels in marrow stromal cells. Confocal microscopy revealed HSF-2 co-localization with HSP-27 in unstimulated cells and HSF-2 nuclear translocation upon FGF-2 stimulation. We further show that FGF-2 stimulation significantly increased the levels of p-STAT-1 in these cells. Western blot analysis confirmed that siRNA suppression of STAT-1 significantly decreased (3.2-fold) RANKL expression and promoter activity in FGF-2 stimulated cells. Chromatin immunoprecipitation (ChIP) assay revealed STAT-1 binding to putative motif located far upstream (-8 kb) in the hRANKL gene promoter region. These results suggest STAT-1 is a

downstream effector of FGF-2 signaling and that elevated levels of FGF-2 stimulates RANKL expression in PDB.

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### Eye Care Services

Guo, A. M., G. Scicli, J. Sheng, J. C. Falck, P. A. Edwards and A. G. Scicli (2009). "20-HETE Can Act as a Non-Hypoxic Regulator of HIF-1{alpha} in Human Microvascular Endothelial Cells." Am J Physiol Heart Circ Physiol **Epub Ahead of Print**. [PDF Full-Text](#)

Henry Ford Health System.

20-HETE increases the expression of Vascular Endothelial Growth Factor (VEGF) in human dermal microvascular endothelial cells (EC). VEGF is regulated by Hypoxia Inducible Factor (HIF-1). We studied whether 20-HETE also upregulates HIF-1alpha using the stable 20-HETE analog WIT003, (20-hydroxyeicosa-5(Z), 14(Z)-dienoic acid, 1-10 microM), and found that it induced a marked increase in VEGF and HIF-1alpha protein levels. The increases in VEGF preceded the changes in HIF-1alpha and a VEGF neutralizing antibody prevented the increases in HIF-1alpha. Stimulation with exogenously added VEGF also led to HIF-1alpha upregulation. This suggests that 20-HETE first causes increases in VEGF, which then causes the upregulation of HIF-1alpha. Addition of WIT003 results in a rapid and sustained increase in superoxide formation. When WIT003 was added in the presence of the NOS inhibitor L-NAME, no changes in superoxide, VEGF, or HIF-1alpha were observed. This suggests that NOS is responsible for the early changes induced by WIT003, likely because of NOS-uncoupling. Furthermore, WIT003 induced the expression of the NADPH oxidase subunit p47(phox) in EC prior to the increases in HIF-1alpha. Incubation with PEG-SOD (400 U/ml), apocynin (100 microM), DPI (10 microM) or p47(phox) down regulation with siRNA all inhibited the increases in HIF-1alpha expression. This indicates that the early changes in superoxide lead to VEGF increases and thereby NADPH oxidase-dependent superoxide production is required for the increases in HIF-1alpha. Incubation with the MEK1/ERK1/2 inhibitor U0126 (10 microM) completely abolishes the increases in VEGF and thus HIF-1alpha, suggesting involvement of ERK1/2 activation. We also found that the higher HIF-1alpha expression induced by WIT003 was accompanied by higher expression of erythropoietin receptor and angiotensin-2 proteins. These increases were caused by HIF-1alpha since their levels were markedly decreased by downregulation of HIF-1alpha with siRNA. 20-HETE may be a novel non-hypoxic regulator of HIF-1alpha, and HIF-1alpha-regulated genes in EC. Key words: Cytochrome P450 4A, Hypoxia inducible factor, Nitric oxide synthase uncoupling, Superoxide.

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### Eye Care Services

Kaufman, S. C. and J. S. Dhaliwal (2009). "Letter to the Editor." Cornea **Epub Ahead of Print**. [Article Request Form](#)

Department of Ophthalmology, Henry Ford Health System, Troy, MI, Department of Ophthalmology, University of Minnesota, Minneapolis, MN, Department of Ophthalmology, Henry Ford Health System, Troy, MI.

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### Family Medicine

Smith, R. C., J. C. Gardiner, Z. H. Luo, S. Schooley, L. Lamerato and K. Rost (2009). "Primary Care Physicians Treat Somatization." Journal of General Internal Medicine **24(7)**: 829-832. [PDF Full-Text](#)

[Smith, Robert C.] B312 Clin Ctr, E Lansing, MI 48824 USA. [Smith, Robert C.; Gardiner, Joseph C.; Luo, Zhehui] Michigan State Univ, E Lansing, MI 48824 USA. [Schooley, Susan; Lamerato, Lois] Henry Ford Hlth Syst, Detroit, MI USA. [Rost, Kathryn] Florida State Univ, Tallahassee, FL 32306 USA.

Smith, RC, B312 Clin Ctr, E Lansing, MI 48824 USA. [Robert.smith@ht.msu.edu](mailto:Robert.smith@ht.msu.edu)

We hypothesized that somatizing patients managed by primary care physicians (PCP) would improve with a relationship-based intervention. We randomized 30 adults with medically unexplained symptoms to treatment or usual care. Four PCPs were trained to intervene with cognitive-behavioral, pharmacological, and patient-centered management and deployed the intervention with seven scheduled visits over 12 months. Outcomes obtained at baseline and 12 months were: Mental component summary (MCS), the primary endpoint, and measures of physical and psychological symptoms and of satisfaction with the PCP. Patients averaged 52.5 years; 83.3% were female; 79.6% were black. Using a difference of differences approach, we found that the intervention produced a large effect size (ES) (0.82; CI: 0.08 to 1.57) for the MCS in the predicted direction, similar to the ES for physical (-0.80; CI: -1.55 to -0.04) and psychological (-1.06; CI: -1.83 to -0.28) improvement and for increased satisfaction with the PCP (0.94; CI: 0.15 to 1.74). Using ANCOVA in a sensitivity analysis, we found that the ES fell slightly (0.59), while other measures were unchanged. Moderate-large effect sizes support the hypothesis that PCPs can effectively treat somatization. This points to the importance of performing a full RCT.

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### **Gastroenterology**

Kwo, P., E. Lawitz, J. McCone, E. Schiff, J. Vierling, D. Pound, M. Davis, J. Galati, S. Gordon, N. Ravendhran, L. Rossaro, F. Anderson, I. Jacobson, R. Rubin, K. Koury, C. Brass, E. Chaudhri and J. Albrecht (2009). "Hcv Sprint-1 Final Results: Svr 24 from a Phase 2 Study of Boceprevir Plus Peginteron (Tm) (Peginterferon Alfa-2b)/Ribavirin in Treatment-Naive Subjects with Genotype-1 Chronic Hepatitis C." Journal of Hepatology **50**: 4. [PDF Full-Text](#)

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### **Gastroenterology**

Lawitz, E., Z. M. Younossi, M. Shiffman, S. Gordon, R. Ghalib, W. Long, A. Muir and J. McHutchison (2009). "Randomized Trial Comparing Systemic and Local Reactions to Controlled-Re Lease Interferon Alpha2b and Pegylated-Interferon Alpha2b in Hepatitis C Patients Who Failed Prior Treatment." Journal of Hepatology **50**: 628. [PDF Full-Text](#)

[Lawitz, E.] Alamo Med Res, San Antonio, TX USA. [Shiffman, M.] Virginia Commonwealth Univ, Div Gastroenterol Hepatol & Nutr, Richmond, VA USA. [Gordon, S.] Henry Ford Hlth Syst, Gastroenterol, Detroit, MI USA. [Ghalib, R.] Methodist Dallas Med Ctr, Dallas, TX USA. [Muir, A.] Duke Univ, Med Ctr, Durham, NC USA. [McHutchison, J.] Duke Clin Res Inst, Durham, NC USA. [wlong@biolix.com](mailto:wlong@biolix.com)

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### **Gastroenterology**

Tuthill, C., S. Verjee, R. Dye, H. Dye, K. Phenis, W. A. Chu, C. Chen, B. Bilir, K. Camacho, S. Gordon, B. Lipson, P. Pockros, A. Sherker, K. Sherman, M. Sjogren, N. Snyder, P. Thuluvath and I. Rios (2009). "Treatment of Hepatitis C with the Immune-Stimulating Dipeptide Scv-07." Journal of Hepatology **50**: 647. [PDF Full-Text](#)

[Tuthill, C.; Phenis, K.; Chu, W. A.; Chen, C.; Rios, I.] SciClone Pharmaceut Inc, Foster City, CA USA. [Verjee, S.] Versante Int Inc, Piedmont, CA USA. [Dye, R.; Dye, H.] Underwood Res, Underwood, WA USA. [Bilir, B.] Arapahoe Gastroenterol, Littleton, CO USA. [Camacho, K.] Accelovance, Peoria, IL USA. [Gordon, S.] Henry Ford Hlth Syst, Detroit, MI USA. [Lipson, B.] Liver Kidney & Internal Med Ctr, Houston, TX USA. [Pockros, P.] Scripps Clin, La Jolla, CA USA. [Sherker, A.] Washington Hosp Ctr, Medstar Res Inst, Washington, DC 20010 USA. [Sherman, K.] Univ Cincinnati, Med Ctr, Cincinnati, OH 45267 USA. [Sjogren, M.] Walter Reed Army Med Ctr, Washington, DC 20307 USA. [Snyder, N.] Univ Texas Med Branch, Galveston, TX USA. [Thuluvath, P.] Johns Hopkins Univ Hosp, Baltimore, MD 21287 USA. [ctuthill@sciclone.com](mailto:ctuthill@sciclone.com)

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### **Hematology, Medical Oncology & Josephine Ford Cancer Center**

Dabak, V., A. Hanbali and P. Kuriakose (2009). "Can rituximab replace splenectomy in immune thrombocytopenic purpura?" Indian Journal of Hematology and Blood Transfusion **25**(1): 6-9. [PDF Full-Text](#)

[Dabak, Vrushali; Hanbali, Amr; Kuriakose, Philip] Henry Ford Hosp, Detroit, MI 48202 USA. Dabak, V, Henry Ford Hosp, 2799 W Grand Blvd, Detroit, MI 48202 USA. [vdabak1@hfhs.org](mailto:vdabak1@hfhs.org)

Aim Immune thrombocytopenic purpura (ITP) is an autoimmune disorder characterized by premature platelet destruction. Standard practice is to initiate treatment with corticosteroids, followed by splenectomy. Most published literature for responses from rituximab is in patients with chronic refractory ITP, who have failed multiple prior treatments, including splenectomy. We therefore decided to analyze our patient population with ITP who had been treated with rituximab, mainly as a second line treatment regimen prior to splenectomy. Methods We performed a retrospective chart review of patients with a diagnosis of ITP who had been treated with rituximab between January 2001 and December 2006 at our institution. Results 18/29 patients (62%) had a CR, 2/29 (7%) patients had a PR, representing an overall response rate of 69%. The average time to response was 5 weeks and all patients have maintained their response for more than 12 months after treatment with rituximab. Conclusion Our study shows higher CR, comparable overall response rates, but with a longer duration of response when compared to the published literature.

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### **Hematology, Medical Oncology & Josephine Ford Cancer Center**

Khaled, Y., M. H. Abidi, N. Janakiraman, K. Kato, J. E. Levine, P. Reddy, M. Medina, E. Peres, A. Hanbali and S. Mineishi (2009). "Outcomes after auto-SCT in African Americans with multiple myeloma." Bone Marrow Transplantation **43**(11): 845-851. [PDF Full-Text](#)

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To study the impact of auto-SCT on the outcomes in African Americans (AA) with multiple myeloma (MM), we evaluated 101 consecutive AA patients who underwent auto-SCT. The median PFS and OS were 15.6 and 50.8 months, respectively. The median OS from diagnosis was 60 months. Traditional pre and post transplant

prognostic variables earlier examined in Caucasian Americans (CA), including beta-2 microglobulin (B2M), chromosome 13 deletion, CR status after auto-SCT, gender, stage, Ig subtype, time to transplant, number of prior regimens and presence of lytic lesions, were not predictive of improved PFS or OS on univariate analysis. Age, lower CD34 cell dose infused, history of palliative radiation therapy (XRT) prior to auto-SCT and refractory disease at the time of auto-SCT were predictive of inferior PFS. History of palliative XRT was the only predictive factor of inferior PFS and OS after auto-SCT on multivariate analysis. In conclusion, MM in AA tends to relapse early after auto-SCT. It is unclear whether early relapses impact OS. Common prognostic peritransplant variables known in CA with MM may not be applicable to AA with MM. Bone Marrow Transplantation (2009) 43, 845-851.

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### **Hypertension & Vascular Research**

Carretero, O. A. and A. Nasjletti (2009). "Juan Carlos Romero, MD 1937-2008 In Memoriam." Hypertension **54**(1): 1-2. [PDF Full-Text](#)

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[Nasjletti, Alberto] New York Med Coll, New York, NY USA.

Carretero, OA, Henry Ford Hosp, Hypertens & Vasc Res Div, Detroit, MI 48202 USA.

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### **Internal Medicine**

Tcheurekdjian, H., S. M. Thyne, L. K. Williams, M. Via, J. R. Rodriguez-Santana, W.

Rodriguez-Cintron, P. C. Avila and E. G. Burchard (2009). "Augmentation of bronchodilator responsiveness by leukotriene modifiers in Puerto Rican and Mexican children." Annals of Allergy Asthma & Immunology **102**(6): 510-517. [PDF Full-Text](#)

[Tcheurekdjian, Haig; Via, Marc; Burchard, Esteban Gonzalez] Univ Calif San Francisco, Dept Med, San Francisco, CA USA. [Tcheurekdjian, Haig; Thyne, Shannon M.] Univ Calif San Francisco, Dept Pediat, San Francisco, CA USA. [Williams, L. Keoki] Henry Ford Hlth Syst, Dept Internal Med, Detroit, MI USA. [Via, Marc; Burchard, Esteban Gonzalez] Univ Calif San Francisco, Inst Human Genet, San Francisco, CA 94143 USA. [Rodriguez-Santana, Jose R.] CSP, Ctr Neumol Pediat, San Juan, PR USA. [Rodriguez-Cintron, William] Vet Caribbean Hlth Care Syst, San Juan, PR USA. [Avila, Pedro C.] Northwestern Univ, Feinberg Sch Med, Div Allergy Immunol, Chicago, IL 60611 USA. [Burchard, Esteban Gonzalez] Univ Calif San Francisco, Dept Biopharmaceut Sci, San Francisco, CA 94143 USA.

Tcheurekdjian, H, Case Western Reserve Univ, Allergy Immunol Associates Inc, 1611 S Green Rd, Ste 231, S Euclid, OH 44121 USA. [haig.tcheurekdjian@gmail.com](mailto:haig.tcheurekdjian@gmail.com)

Background: Ethnic-specific interactions between different asthma medications are not well described.

Objective: To determine whether the use of leukotriene modifiers is associated with the magnitude of bronchodilator responsiveness among Mexican American and Puerto Rican children with persistent asthma.

Methods: A cross-sectional study of 84 Mexican American and 192 Puerto Rican children with persistent asthma who were aged 8 to 16 years. Within each group, bronchodilator responsiveness to albuterol, objectively assessed via spirometry, was compared between participants using leukotriene modifiers and those not using leukotriene modifiers. Results: Leukotriene modifier use was associated with a clinically significant increase in percentage change in forced expiratory volume in 1 second of 11.8 (P<.001) in Puerto Rican children, but there was no significant change in percentage change in forced expiratory volume in 1 second (-3.2, P=.57) in Mexican American children. This finding persisted after controlling for the use of inhaled corticosteroids. In addition, among the Puerto Rican children, the association between leukotriene modifier use and augmented bronchodilator responsiveness was greatest in those younger than 12 years. Conclusions: Among children with persistent asthma, use of leukotriene modifiers is associated with augmented bronchodilator responsiveness to albuterol in Puerto Ricans, but not Mexican Americans. This ethnic-specific, drug-drug interaction highlights the need for the further understanding of asthma pharmacogenetics among children from different ethnic groups to improve asthma outcomes. Ann Allergy Asthma Immunol. 2009; 102:510-517.

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## Neurology

Athiraman, H., Q. Jiang, G. L. Ding, L. Zhang, Z. G. Zhang, L. Wang, A. S. Arbab, Q. Li, S. Panda, K. Ledbetter, A. M. Rad and M. Chopp (2009). "Investigation of relationships between transverse relaxation rate, diffusion coefficient, and labeled cell concentration in ischemic rat brain using MRI." Magn Reson Med **61**(3): 587-94. [PDF Full-Text](#)

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

MRI has been used to evaluate labeled cell migration and distribution. However, quantitative determination of labeled cell concentration using MRI has not been systematically investigated. In the current study, we investigated the relationships between labeled cell concentration and MRI parameters of transverse relaxation rate,  $R(2)$ , and apparent diffusion coefficient (ADC), in vitro in phantoms and in vivo in rats after stroke. Significant correlations were detected between iron concentration or labeled cell concentration and MRI measurements of  $R(2)$ , ADC, and  $ADC \times R(2)$  in vitro. In contrast, in vivo labeled cell concentration did not significantly correlate with  $R(2)$ , ADC, and  $ADC \times R(2)$ . A major factor for the absence of a significant correlation between labeled cell concentration and MRI measurements in vivo may be attributed to background effects of ischemic tissue. By correcting the background effects caused by ischemic damage,  $\Delta R(2)$  (difference in  $R(2)$  values in the ischemic tissue with and without labeled cells) exhibited a significant correlation to labeled cell concentration. Our study suggests that MRI parameters have the potential to quantitatively determine labeled cell concentration in vivo.

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## Neurology

Evans, R. W. and P. D. Mitsias (2009). "Headache at onset of acute cerebral ischemia." Headache **49**(6): 902-8. [PDF Full-Text](#)

Stroke and Neurovascular Center, Department of Neurology, K-11, Henry Ford Hospital, 2799 West Grand Boulevard, Detroit, MI 48202, USA.

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## Neurology

Hacein-Bey, L. and P. N. Varelas (2009). "Pedunculated Basilar Terminus Aneurysm with Pseudo-Septation due to Anterior Herniation through a Perforated Membrane of Lilliequist." AJNR Am J Neuroradiol **Epub Ahead of Print**. [PDF Full-Text](#)

Departments of Radiology, Neurosurgery, and Neurology, Medical College of Wisconsin, Milwaukee, Wis; and Departments of Neurology and Neurosurgery, Henry Ford Hospital, Detroit, Mich.

SUMMARY: Septations within cerebral arteries or aneurysms are exceedingly rare in the absence of associated fenestrations. We report an unusual unruptured pedunculated basilar apex aneurysm, with a "pseudoseptation" between the main aneurysmal sac and an anterior compartment, which was, in fact, represented by a perforation in the membrane of Lilliequist, permitting anterior aneurysmal herniation into the carotid-chiasmatic cistern. The patient was successfully treated with detachable coils. This case is unusual on 2 accounts: 1) the aneurysm's appearance, and 2) the presence of a large fenestration in the membrane of Lilliequist, of which anatomic features are herein reviewed.

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## Neurology

Katakowski, M., F. Jiang, X. Zheng, J. A. Gutierrez, A. Szalad and M. Chopp (2009). "Tumorigenicity of cortical astrocyte cell line induced by the protease ADAM17." Cancer Sci **Epub Ahead of Print**. [PDF Full-Text](#)

Department of Neurology, Henry Ford Hospital, Detroit, Michigan.

The metalloprotease ADAM17 (a.k.a. TACE) plays a pivotal role in the cleavage and activation of membrane-anchored receptor ligands. More recently, it has been revealed that ADAM17 is a potent sheddase of the epidermal growth factor (EGF) family of ligands and regulates epidermal growth factor receptor (EGFR) activity in a variety of tumors. EGFR is a key component of autonomous growth signaling in several tumors, and correlates with the malignancy grade of astrocytoma. In this study, we tested the hypothesis that over-expression of ADAM17 in cortical astrocytes derived from normal brain would induce a progression towards a malignant phenotype. Over-expression of human ADAM17 (hADAM17) in the CTX-TNA2 cortical astrocyte cell line resulted in non-adherent growth, increased proliferation, invasiveness, production of angiogenic factors, and expression of genes associated with immature and/or neoplastic cells. hADAM17 up-regulated EGFR and AKT phosphorylation, and increased proliferation and cell invasion were significantly dependent upon EGFR activity. When implanted in the nude mouse brain, CTX-TNA2 cells induced low histological grade, benign intraventricular gliomas. In contrast, the same astrocytes with hADAM17 formed large malignant gliomas. Taken together, these findings suggest that unregulated ADAM17 activity induces functional changes in astrocytes that significantly advance the malignant phenotype. (Cancer Sci 2009).

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### Neurology

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

Henry Ford Health System, United States.

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

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### Neurology

Liu, Z., R. L. Zhang, Y. Li, Y. Cui and M. Chopp (2009). "Remodeling of the corticospinal innervation and spontaneous behavioral recovery after ischemic stroke in adult mice." [Stroke 40\(7\): 2546-51. PMC2704262. PDF Full-Text](#)

Department of Neurology, Henry Ford Hospital, Detroit, MI 48202, USA.

**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.

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## Neurology

Zhang, J., Y. Li, Z. G. Zhang, M. Lu, J. Borneman, B. Buller, S. Savant-Bhonsale, S. B. Elias and M. Chopp (2009). "Bone marrow stromal cells increase oligodendrogenesis after stroke." J Cereb Blood Flow Metab **29**(6): 1166-74. [Article Request Form](#)

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

Oligodendrocytes are sensitive to ischemic damage. The Sonic hedgehog (Shh) pathway is critical in oligodendrogenesis; Gli1 is the principal effector of Shh signaling. We investigated oligodendrogenesis and Shh/Gli1 pathway activation after bone marrow stromal cell (BMSC) treatment of stroke in rats. Rats were subjected to the middle cerebral artery occlusion (MCAo). BMSCs have been shown to promote functional recovery post stroke. A therapeutic dose of BMSC (3 x 10<sup>6</sup>) cells treatment was initiated 1 day after MCAo. Immunohistochemistry was carried out to measure the oligodendrocyte progenitor cells, oligodendrocytes, myelin, and expressions of Shh and Gli1 at 14 days after MCAo. Gene expression of Shh and Gli1 was tested at 2 days after MCAo. An in vitro study was used to investigate the effects of BMSC on a premature oligodendrocyte cell line (N20.1 cells). BMSC treatment significantly increased O4(+) oligodendrocytes, MBP(+) area, and bromodeoxyuridine (BrdU)(+), NG2(+), BrdU(+)-NG2(+) cells, and mRNA and protein expressions of Shh and Gli1 in the ipsilateral brain of the MCAo rats than that in phosphate buffered saline (PBS)-treated rats. BMSCs promoted N20.1 cell proliferation and Gli1 mRNA expression, and these effects were abolished by the Shh pathway inhibitor cyclopamine. These data indicate that the BMSC treatment stimulates oligodendrogenesis by activation of the Shh/Gli1 pathway post stroke.

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## Neurosurgery

Chopp, M., A. Mahmood, D. Y. Lu and Y. Li (2009). "Mesenchymal stem cell treatment of traumatic brain injury." Journal of Neurosurgery **110**(6): 1186-1187. [PDF Full-Text](#)

[Chopp, Michael] Henry Ford Hlth Syst, Dept Neurol, Detroit, MI USA. Henry Ford Hlth Syst, Dept Neurosurg, Detroit, MI USA.

Chopp, M, Henry Ford Hlth Syst, Dept Neurol, Detroit, MI USA.

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## Neurosurgery

Gusarova, G. A., L. A. Dada, A. M. Kelly, C. Brodie, L. A. Witters, N. S. Chandel and J. I. Sznajder (2009). "alpha 1-AMP-Activated Protein Kinase Regulates Hypoxia-Induced Na,K-ATPase Endocytosis via Direct Phosphorylation of Protein Kinase C zeta." Molecular and Cellular Biology **29**(13): 3455-3464. [Article Request Form](#)

[Gusarova, Galina A.; Dada, Laura A.; Kelly, Aileen M.; Chandel, Navdeep S.; Sznajder, Jacob I.] Northwestern Univ, Feinberg Sch Med, Div Pulm & Crit Care Med, Chicago, IL 60611 USA. [Brodie, Chaya] Henry Ford Hlth Syst, Dept Neurosurg, Detroit, MI USA.

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Hypoxia promotes Na,K-ATPase endocytosis via protein kinase C zeta (PKC zeta)-mediated phosphorylation of the Na,K-ATPase alpha subunit. Here, we report that hypoxia leads to the phosphorylation of 5'-AMP-activated protein kinase (AMPK) at Thr172 in rat alveolar epithelial cells. The overexpression of a dominant-negative AMPK alpha subunit (AMPK-DN) construct prevented the hypoxia-induced endocytosis of Na,K-ATPase. The overexpression of the reactive oxygen species (ROS) scavenger catalase prevented hypoxia-induced AMPK activation. Moreover, hypoxia failed to activate AMPK in mitochondrion-deficient rho(0)-A549 cells, suggesting that mitochondrial ROS play an essential role in hypoxia-induced AMPK activation. Hypoxia-induced PKC zeta translocation to the plasma membrane and phosphorylation at Thr410 were prevented by the pharmacological inhibition of AMPK or by the overexpression of the AMPK-DN construct. We found that AMPK alpha phosphorylates PKC zeta on residue Thr410 within the PKC zeta activation loop. Importantly, the activation of AMPK alpha was necessary for hypoxia-induced AMPK-PKC zeta binding in alveolar epithelial cells. The overexpression of T410A mutant PKC zeta prevented hypoxia-induced Na,K-ATPase endocytosis, confirming that PKC zeta Thr410 phosphorylation is essential for this process. PKC zeta activation by AMPK is isoform specific, as small interfering RNA targeting the alpha 1 but not the alpha 2 catalytic subunit prevented PKC zeta activation. Accordingly, we provide the first evidence that hypoxia-generated mitochondrial ROS lead to the activation of the AMPK alpha 1 isoform, which binds and directly phosphorylates PKC zeta at Thr410, thereby promoting Na,K-ATPase endocytosis.

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## Neurosurgery

Hong, X., C. Miller, S. Savant-Bhonsale and S. N. Kalkanis (2009). "Antitumor treatment using interleukin-12-secreting marrow stromal cells in an invasive glioma model."

Neurosurgery 64(6): 1139-46; discussion 1146-7. [PDF Full-Text](#)

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

**OBJECTIVE:** Marrow stromal cells (MSCs) have the potential to migrate toward sites of injury or disease in the central nervous system. Encouraging results have been obtained by using MSCs to deliver therapeutic molecules. However, most brain tumor animal models--unlike in actual human disease states--use cells with limited invasion properties. In the present study, C57/B16 mice were implanted with the highly invasive Ast11.9-2 glioma cell line to investigate the potential therapeutic effects of interleukin-12 (IL-12)-secreting MSCs. **METHODS:** MSCs were infected with adenovirus encoding murine IL-12 (AdIL12). The infection conditions were optimized by determination of cytotoxicity and IL-12 secretion after AdIL12 infection in vitro. After implanting Ast11.9-2 tumor into mouse brain, we conducted a survival experiment to compare 4 distinct treatment groups by injecting culture medium control (sham), MSCs alone, MSCs infected with control virus (MSC-adenovirus encoding green fluorescent protein), and MSCs infected with IL-12-expressing virus (MSC-AdIL12) in the peritumoral region of the brain. Tumor tissues were analyzed by hematoxylin and eosin staining. IL-12 expression was analyzed by immunohistochemistry staining. Y chromosome fluorescent in situ hybridization was used to detect injected MSCs. Cell populations of CD57 (natural killer cells), CD3 (total T cells), and 7-AAD (dead cells) in whole brain tissue were analyzed by fluorescence-activated cell sorting at days 4 and 7 after therapeutic treatment. **RESULTS:** Serum IL-12 increased significantly at days 4 and 7 after MSC-AdIL12 implantation. IL-12-expressing cells were detected by immunohistochemistry staining and Y chromosome-positive staining cells were found in the tumor area, confirming successful IL-12 delivery. MSC-AdIL12 treatment yielded increased natural killer cell infiltration in brain tissue at day 4, leading to an expected increase in nonspecific cell death, while total T-cell counts remained unchanged. MSC-IL-12 treatment extended animal survival but did not result in a statistically significant difference in comparison to other groups. Because all animals ultimately died of the brain tumors, MSC-AdIL12 treatment did not completely arrest the invasive growth pattern of these lesions. **CONCLUSION:** The results indicate that MSCs may serve as useful delivery vehicles for IL-12 and other antineoplastic agents in brain tumor therapy.

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## Neurosurgery

Torcuator, R., R. Zuniga, R. Loutfi and T. Mikkelsen (2009). "Bevacizumab and irinotecan treatment for progressive diffuse brainstem glioma: case report." Journal of Neuro-Oncology **93**(3): 409-412. [PDF Full-Text](#)

[Torcuator, Roy; Zuniga, Richard; Mikkelsen, Tom] Henry Ford Hlth Syst, Hermelin Brain Tumor Ctr, Dept Neurosurg, Detroit, MI 48202 USA. [Loutfi, Randa] Henry Ford Hlth Syst, Hermelin Brain Tumor Ctr, Dept Med Oncol, Detroit, MI 48202 USA. [Mikkelsen, Tom] Henry Ford Hlth Syst, Hermelin Brain Tumor Ctr, Dept Neurol, Detroit, MI 48202 USA. Torcuator, R, Henry Ford Hlth Syst, Hermelin Brain Tumor Ctr, Dept Neurosurg, 2799 W Grand Blvd, Detroit, MI 48202 USA. [nsroy@neuro.hfh.edu](mailto:nsroy@neuro.hfh.edu)

Diffuse brainstem glioma carries a dismal prognosis. The current cornerstone of treatment is radiation therapy. Chemotherapy appears to be ineffective and the role of this treatment in the recurrent or progressive setting is not known. Bevacizumab and irinotecan have been reported to have shown radiographic response and improvement in progression-free survival among patients with malignant supratentorial gliomas. In this paper, we report our experience in an adult patient with progressive diffuse brainstem glioma treated with bevacizumab and irinotecan.

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### **Obstetrics & Gynecology**

Collins-Fulea, C. (2009). "Models of organizational structure of midwifery practices located in institutions with residency programs." J Midwifery Womens Health **54**(4): 287-93. [PDF Full-Text](#)

Henry Ford Health System, Detroit, Michigan 48202, USA. [cfulea@cogeco.ca](mailto:cfulea@cogeco.ca)

Four models of organizational structure for midwifery practices that are located in academic institutions with residency programs are described: parallel models, coexistence models, fully integrated models, and blended models. Examples of each of these models are presented along with advantages and disadvantages and overall effect on resident education.

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### **Other**

Gerlach, M. A. (2009). "POSTOPERATIVE VISUAL ANALOG SCALE (VAS) RESULTS AND OTHER ADVANTAGES USING AN OSTOMY POUCH ADAPTOR(star)." Journal of Wound Ostomy and Continence Nursing **36**(3): S43-S43. [PDF Full-Text](#)

[Gerlach, Mary A.] Henry Ford Macomb Hosp, Clinton Township, MI USA. [gerlachm@hfhs.org](mailto:gerlachm@hfhs.org)

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### **Otolaryngology**

Rosenthal, L. H. S., M. S. Benninger, C. H. Stone and M. A. Zacharek (2009). "Wound healing in the rabbit paranasal sinuses after Coblation: Evaluation for use in endoscopic sinus surgery." American Journal of Rhinology & Allergy **23**(3): 360-363. [Article Request Form](#)

[Rosenthal, Laura H. Swibel; Zacharek, Mark A.] Henry Ford Hosp, Dept Otolaryngol Head & Neck Surg, Detroit, MI USA. [Stone, Chad H.] Henry Ford Hosp, Dept Pathol & Lab Med, Detroit, MI USA. [Benninger, Michael S.] Cleveland Clin, Head & Neck Inst, Cleveland, OH 44106 USA.

Rosenthal, LHS, Henry Ford Hosp, Dept Otolaryngol K8, 2799 W Grand Blvd, Detroit, MI 48202 USA. [lrosenthal@alumni.upenn.edu](mailto:lrosenthal@alumni.upenn.edu)

Background: Bipolar radiofrequency can be used surgically to excise and cauterize tissue simultaneously. It has potential for use in endoscopic sinus surgery (ESS). This study was performed to determine the extent and pattern of injury in the paranasal sinuses with bipolar radiofrequency and evaluate wound healing. Methods: Eight rabbits underwent Coblation of maxillary sinus mucosa with biopsy immediately, on postoperative day (POD) 3, 7, 14, or 29. Maxillary mucosa was exposed through the nasal dorsum, and a Coblator PROciseXP wand used on a power setting of 7 for 2 seconds. Three of the rabbits also had Coblation of ethmoid mucosa over the lamina papyracea, after extending the maxillary ostomy, with biopsy immediately. Results: Coblation resulted in immediate loss of surface respiratory epithelium and thermal-type injury to the underlying seromucinous glands. On POD 3, the site showed reepithelialization with squamous metaplastic epithelium. The seromucinous glands underwent coagulative necrosis. At POD 7, there was partial replacement of overlying epithelium by respiratory epithelium. The underlying seromucinous glands were lost and replaced by fibroblastic proliferation, with less fibrosis than the mechanically created ostomy site. The underlying bone had reactive, regenerative changes. On PODs 14 and 29, there was further regeneration of respiratory epithelium. Fibrosis was mild. Coblation resulted in gross violation of the bony wall in one maxillary sinus. There were no histological changes in the orbit. Conclusion: Rabbit paranasal sinus mucosa heals appropriately after Coblation injury. (Am J Rhinol Allergy 23, 360-363, 2009; doi: 10.2500/ajra.2009.23.3326)

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### Otolaryngology

Sethi, S., M. S. Benninger, M. Lu, S. Havard and M. J. Worsham (2009). "Noninvasive Molecular Detection of Head and Neck Squamous Cell Carcinoma An Exploratory Analysis." Diagnostic Molecular Pathology 18(2): 81-87. [PDF Full-Text](#)

[Sethi, Seema; Benninger, Michael S.; Lu, Mei; Havard, Shalita; Worsham, Maria J.] Henry Ford Hosp, Dept Otolaryngol & Biostat, Detroit, MI 48202 USA.

Sethi, S, Henry Ford Hosp, Dept Otolaryngol & Biostat, 1 Ford Pl 1D, Detroit, MI 48202 USA. [ssethi1@hfhs.org](mailto:ssethi1@hfhs.org)

Background: Head and neck squamous cell carcinoma (HNSCC) is a heterogeneous disease evolving through multistep carcinogenesis, one of the steps being genetic alterations. Noninvasive identification of HNSCC-specific genetic alterations using saliva would have immense potential in early diagnosis and screening, particularly among high-risk patients. Design: In this exploratory Study, a prospective cohort of 27 HNSCC and 10 healthy controls was examined to determine whether genetic alterations (losses and gains) in saliva DNA differentiated HNSCC patients from normal controls. Saliva DNA was interrogated by a candidate gene panel comprising 82 genes using the multiplex ligation-dependent probe amplification assay. Results: Eleven genes showed some predictive ability in identifying HNSCC cases from normal controls: PMAIP1, PTPN1, ERBB2, ABCC4, UTY, DNMT1, CDKN2B, CDKN2D, NFKB1, TP53, and DCC. Statistical analysis using the Classification and Regression Tree (CART) identified 2 genes, PMAIP1 and PTPN1, which correctly discriminated all 27 HNSCC patients (100%) from normal controls. Results were validated using the leave-one-out validation approach. Conclusions: Noninvasive high-throughput multiplex ligation-dependent probe amplification identified discrete gene signatures that differentiated HNSCC patients from normal controls providing proof-of-concept for noninvasive HNSCC detection.

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### Otolaryngology

Stach, B. A., B. W. Y. Hornsby, M. A. L. Rosenfeld and A. R. DeChicchis (2009). "The complexity of auditory aging." Semin Hear 30(2): 84-111. [Article Request Form](#)

Henry Ford Hospital, Detroit, MI 48202

Age-related decline in hearing is the result of complex changes in audibility, suprathreshold processing, and cognition. Changes in cochlear structures, whether from biological aging of the structures themselves or secondary to intrinsic and extrinsic influences that occur with the passage of time, result in hearing sensitivity loss. The outward expression of the underlying disorder is fairly consistent. That is, loss of function of cochlear hair cells and other structures consistently manifest hearing sensitivity loss and the consequent deficits in audibility. Age-related changes in auditory nervous system structures may also play a role in overall hearing capability, although the outward expression of the disorder is likely to be subtler than cochlear loss in a given

individual and considerably more variable among individuals. Regardless, the complex hearing disorder associated with the aging process can have a significant impact on overall wellness. This review article provides an overview of aging and age-related decline in audition, with an emphasis on speech perceptual deficits with aging.

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### **Otolaryngology**

Swibel Rosenthal, L. H., M. S. Benninger, C. H. Stone and M. A. Zacharek (2009). "Wound healing in the rabbit paranasal sinuses after Coblation: Evaluation for use in endoscopic sinus surgery." Am J Rhinol Allergy **23**(3): 360-3. [Article Request Form](#)

Department of Otolaryngology-Head and Neck Surgery, Henry Ford Hospital, Detroit, Michigan.

**BACKGROUND:** Bipolar radiofrequency can be used surgically to excise and cauterize tissue simultaneously. It has potential for use in endoscopic sinus surgery (ESS). This study was performed to determine the extent and pattern of injury in the paranasal sinuses with bipolar radiofrequency and evaluate wound healing. **METHODS:** Eight rabbits underwent Coblation of maxillary sinus mucosa with biopsy immediately, on postoperative day (POD) 3, 7, 14, or 29. Maxillary mucosa was exposed through the nasal dorsum, and a Coblator PROciseXP wand used on a power setting of 7 for 2 seconds. Three of the rabbits also had Coblation of ethmoid mucosa over the lamina papyracea, after extending the maxillary ostomy, with biopsy immediately. **RESULTS:** Coblation resulted in immediate loss of surface respiratory epithelium and thermal-type injury to the underlying seromucinous glands. On POD 3, the site showed reepithelialization with squamous metaplastic epithelium. The seromucinous glands underwent coagulative necrosis. At POD 7, there was partial replacement of overlying epithelium by respiratory epithelium. The underlying seromucinous glands were lost and replaced by fibroblastic proliferation, with less fibrosis than the mechanically created ostomy site. The underlying bone had reactive, regenerative changes. On PODs 14 and 29, there was further regeneration of respiratory epithelium. Fibrosis was mild. Coblation resulted in gross violation of the bony wall in one maxillary sinus. There were no histological changes in the orbit. **CONCLUSION:** Rabbit paranasal sinus mucosa heals appropriately after Coblation injury.

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### **Otolaryngology**

Syamal, M. N. and G. M. Gardner (2009). "Operative adaptation for endoscopic identification of Zenker's diverticulum." Laryngoscope **119**(5): 861-3. [PDF Full-Text](#)

Department of Otolaryngology-Head and Neck Surgery, Henry Ford Health System, Wayne State University School of Medicine, Detroit, Michigan 48202, USA.

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### **Otolaryngology**

Yaremchuk, K. and J. D. Clark (2009). "A clearer divide: Henry Ford's policy combats conflicts of interest." Mod Healthc **39**(20): 26. [Article Request Form](#)

Vice President of Clinical Practice Performance, Henry Ford Health System.

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### **Pathology**

Anagli, J., Y. X. Han, L. Stewart, D. M. Yang, A. Movsisyan, K. Abounit and D. Seyfried (2009). "A novel calpastatin-based inhibitor improves postischemic neurological recovery." Biochemical and Biophysical Research Communications **385**(1): 94-99. [PDF Full-Text](#)

[Anagli, John; Stewart, Laura; Movsisyan, Ashkhen; Abounit, Kadija] Henry Ford Hosp, Dept Pathol, Detroit, MI 48202 USA. [Han, Yuxia; Yang, Dongmei; Seyfried, Donald] Henry Ford Hosp, Dept Neurosurg, Detroit, MI 48202 USA.

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Calpastatin, a naturally occurring protein, is the only inhibitor that is specific for calpain. A novel blood-brain barrier (BBB)-permeant calpastatin-based calpain inhibitor, named B27-HYD, was developed and used to assess calpain's contribution to neurological dysfunction after stroke in rats. Posts ischemic administration of B27-HYD reduced infarct volume and neurological deficits by 35% and 44%, respectively, compared to untreated animals. We also show that the pharmacologic intervention has engaged the intended biologic target. Our data further demonstrates the potential utility of SBDP145, a signature biomarker of acute brain injury, in evaluating possible mechanisms of calpain in the pathogenesis of stroke and as an adjunct in guiding therapeutic decision making. (C) 2009 Elsevier Inc. All rights reserved.

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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." Obes Surg **EPub Ahead of Print**.  
[PDF Full-Text](#)

Department of Pathology and Laboratory Medicine, Henry Ford Hospital, 2799 West Grand Boulevard, Detroit, MI, 48202, USA, [hlee1@hfhs.org](mailto:hlee1@hfhs.org).

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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## Pulmonary & Critical Care Medicine

Rehman, A., R. Iscimen, M. Yilmaz, H. Khan, J. Belsher, J. F. Gomez, A. C. Hanson, B. Afessa, T. H. Baron, Sr. and O. Gajic (2009). "Prophylactic endotracheal intubation in critically ill patients undergoing endoscopy for upper GI hemorrhage." Gastrointest Endosc **69**(7): e55-9. [PDF Full-Text](#)

Division of Pulmonary and Critical Care Medicine, Mayo Clinic, Rochester, Minnesota 55905, USA. [arehman1@hfhs.org](mailto:arehman1@hfhs.org)

BACKGROUND: Cardiopulmonary complications are common after endoscopy for upper GI (UGI) hemorrhage in the intensive care unit (ICU). OBJECTIVE: To evaluate the practice and outcome of elective prophylactic endotracheal intubation before endoscopy for UGI hemorrhage in the ICU. DESIGN: Retrospective, propensity-matched case-control study. SETTING: A 24-bed medical ICU in a tertiary center. PATIENTS: ICU patients who underwent endoscopy for UGI hemorrhage. MAIN OUTCOME MEASUREMENTS: Cardiopulmonary complications, ICU and hospital length of stay, and mortality. In a propensity analysis, patients who were intubated for airway protection before UGI endoscopy were matched by probability of intubation to controls who were not intubated before UGI endoscopy. RESULTS: Of 307 patients, 53 underwent elective prophylactic intubation before UGI endoscopy. The probability of intubation depended on the Acute Physiology and Chronic Health Evaluation III (APACHE III) score (OR 1.4; 95% CI, 1.2-1.6), age (OR 0.97; 95% CI, 0.95-0.99), the presence of hematemesis (OR 1.9; 95% CI, 0.8-5.1), previous lung disease (OR 2.1; 95% CI, 0.8-4.9), and the number of transfusions (OR 1.1; 95% CI, 1.0-1.1 per unit). Nonintubated matched controls were identified for all but 4 patients with active massive hematemesis, who were excluded from matched analysis. Cumulative incidence of cardiopulmonary complications (53% vs 45%, P = .414), ICU

length of stay (median 2.2 vs 1.8 days,  $P = .138$ ), hospital length of stay (6.9 vs 5.9 days,  $P = .785$ ), and hospital mortality (14% vs 20%,  $P = .366$ ) were similar. CONCLUSIONS: Cardiopulmonary complications are frequent after endoscopy for acute UGI bleeding in ICU patients and are largely unaffected by the practice of prophylactic intubation.

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### **Pulmonary & Critical Care Medicine**

Shakoor, H., S. Murthy, D. Mason, D. Johnston, S. S. Shah, M. C. Carrillo and A. C. Mehta (2009). "Lobar Torsion After Lung Transplantation-A Case Report and Review of the Literature." Artificial Organs **33**(7): 551-553. [PDF Full-Text](#)

[Shakoor, Hasan; Shah, Sonia S.; Mehta, Atul C.] Cleveland Clin Fdn, Dept Pulm Dis, Cleveland, OH 44195 USA. [Shakoor, Hasan; Shah, Sonia S.; Mehta, Atul C.] Cleveland Clin Fdn, Dept Crit Care Med, Cleveland, OH 44195 USA. [Murthy, Sudish; Mason, David; Johnston, Douglas] Cleveland Clin Fdn, Dept Thorac & Cardiovasc Surg, Cleveland, OH 44195 USA. [Carrillo, Maria C.] Henry Ford Hosp, Dept Pulm & Crit Care Med, Detroit, MI 48202 USA.

Mehta, AC, Cleveland Clin Fdn, Dept Pulm Allergy & Crit Care Med, 9500 Euclid Ave,A90, Cleveland, OH 44195 USA. [mehtaa1@ccf.org](mailto:mehtaa1@ccf.org)

Lobar torsion is a rare complication following lung transplantation. Early detection and immediate therapeutic intervention can lead to a favorable outcome. We report an unusual case of left lingular torsion following single lung transplantation performed for idiopathic pulmonary fibrosis. The patient experienced severe ventilatory compromise immediately after leaving the operating room, and a chest X-ray revealed a well-demarcated area of consolidation involving the left mid- and lower lung zones. Lingular torsion was promptly diagnosed and corrected surgically. The possibility of acute lobar torsion should be considered in lung transplant recipients who experience acute respiratory compromise in the early postoperative period. Early diagnosis and correction can avoid pulmonary infarction and the need for lobar resection.

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### **Radiation Oncology**

Brown, S. L., A. Rodger and C. G. Orton (2009). "Hypofractionation is a proven safe and effective modality for postoperative whole-breast radiotherapy for early breast cancer patients." Medical Physics **36**(6): 1927-1930. [Article Request Form](#)

[Brown, Stephen L.] Henry Ford Hosp, Detroit, MI 48202 USA. [Brown, Stephen L.] Wayne State Univ, Sch Med, Detroit, MI 48202 USA. [Rodger, Alan] Kelvingrove, Glasgow G3 7LW, Lanark, Scotland.

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### **Radiation Oncology**

Liu, D., M. Ajlouni, J. Y. Jin, S. Ryu, F. Siddiqui, A. Patel, B. Movsas and I. J. Chetty (2009). "Analysis of outcomes in radiation oncology: an integrated computational platform." Med Phys **36**(5): 1680-9. [PDF Full-Text](#)

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Radiotherapy research and outcome analyses are essential for evaluating new methods of radiation delivery and for assessing the benefits of a given technology on locoregional control and overall survival. In this article, a computational platform is presented to facilitate radiotherapy research and outcome studies in radiation oncology. This computational platform consists of (1) an infrastructural database that stores patient diagnosis, IMRT treatment details, and follow-up information, (2) an interface tool that is used to import and export IMRT

plans in DICOM RT and AAPM/RTOG formats from a wide range of planning systems to facilitate reproducible research, (3) a graphical data analysis and programming tool that visualizes all aspects of an IMRT plan including dose, contour, and image data to aid the analysis of treatment plans, and (4) a software package that calculates radiobiological models to evaluate IMRT treatment plans. Given the limited number of general-purpose computational environments for radiotherapy research and outcome studies, this computational platform represents a powerful and convenient tool that is well suited for analyzing dose distributions biologically and correlating them with the delivered radiation dose distributions and other patient-related clinical factors. In addition the database is web-based and accessible by multiple users, facilitating its convenient application and use.

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## **Radiation Oncology**

Sprangers, M. A. G., J. A. Sloan, R. Veenhoven, C. S. Cleeland, M. Y. Halyard, A. R. Abertnethy, F. Baas, A. M. Barsevick, M. Bartels, D. I. Boomsma, C. Chauhan, A. C. Dueck, M. H. Frost, P. Hall, P. Klepstad, N. G. Martin, C. Miaskowski, M. Mosing, B. Movsas, C. J. F. Van Noorden, D. L. Patrick, N. L. Pedersen, M. E. Ropka, Q. L. Shi, G. Shinozaki, J. A. Singh, P. Yang and A. H. Zwinderman (2009). "The Establishment of the GENEQOL Consortium to Investigate the Genetic Disposition of Patient-Reported Quality-of-Life Outcomes." *Twin Research and Human Genetics* 12(3): 301-311. [Article Request Form](#)

[Sprangers, Mirjam A. G.] Univ Amsterdam, Acad Med Ctr, Dept Med Psychol, NL-1105 AZ Amsterdam, Netherlands. [Sloan, Jeff A.] Mayo Clin, Dept Hlth Sci Res, Rochester, MN USA. [Veenhoven, Ruut] Erasmus Univ, Fac Social Sci, Rotterdam, Netherlands. [Cleeland, Charles S.; Shi, Quiling] Univ Texas MD Anderson Canc Ctr, Dept Symptom Res, Houston, TX 77030 USA. [Halyard, Michele Y.] Mayo Clin, Dept Radiat Oncol, Scottsdale, AZ USA. [Abertnethy, Amy R.] Duke Univ, Med Ctr, Duke Canc Care Res Program, Durham, NC USA. [Baas, Frank] Univ Amsterdam, Acad Med Ctr, Neurogenet Lab, NL-1105 AZ Amsterdam, Netherlands. [Barsevick, Andrea M.] Fox Chase Canc Ctr, Philadelphia, PA 19111 USA. [Bartels, Meike; Boomsma, Dorret I.] Vrije Univ Amsterdam, Dept Biol Psychol, Amsterdam, Netherlands. [Chauhan, Cynthia] Canc Advocay, Wichita, KS USA. [Dueck, Amylou C.] Mayo Clin, Biostat Sect, Scottsdale, AZ USA. [Frost, Marlene H.] Mayo Clin, Womens Canc Program, Rochester, MN USA. [Hall, Per; Pedersen, Nancy L.] Karolinska Inst, Dept Med Epidemiol & Biostat, Stockholm, Sweden. [Klepstad, Pal] Norwegian Univ Sci & Technol, St Olav Univ Hosp, Dept Intens Care Med, N-7034 Trondheim, Norway. [Martin, Nicholas G.; Mosing, Miriam] Queensland Inst Med Res, Brisbane, Qld 4006, Australia. [Miaskowski, Christine] Univ Calif San Francisco, Sch Nursing, San Francisco, CA 94143 USA. [Movsas, Benjamin] Henry Ford Hlth Syst, Dept Radiat Oncol, Detroit, MI USA. [Van Noorden, Cornelis J. F.] Univ Amsterdam, Acad Med Ctr, Dept Cell Biol & Histol, NL-1105 AZ Amsterdam, Netherlands. [Patrick, Donald L.] Univ Washington, Dept Hlth Serv, Seattle, WA 98195 USA. [Ropka, Mary E.] Fox Chase Canc Ctr, Canc Prevent & Control Program, Cheltenham, PA USA. [Shinozaki, Gen] Mayo Clin, Dept Psychiat & Psychol, Rochester, MN USA. [Singh, Jasvinder A.] Minneapolis Vet Affairs Med Ctr, Minneapolis, MN USA. [Singh, Jasvinder A.] Univ Minnesota, Minneapolis, MN USA. [Singh, Jasvinder A.] Mayo Clin, Coll Med, Rochester, MN USA. [Yang, Ping] Mayo Clin, Dept Genet Epidemiol, Rochester, MN USA. [Zwinderman, Ailko H.] Univ Amsterdam, Acad Med Ctr, Dept Clin Epidemiol & Biostat, NL-1105 AZ Amsterdam, Netherlands.

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To our knowledge, no comprehensive, interdisciplinary initiatives have been taken to examine the role of genetic variants on patient-reported quality-of-life outcomes. The overall objective of this paper is to describe the establishment of an international and interdisciplinary consortium, the GENEQOL Consortium, which intends to investigate the genetic disposition of patient-reported quality-of-life outcomes. We have identified five primary patient-reported quality-of-life outcomes as initial targets: negative psychological affect, positive

psychological affect, self-rated physical health, pain, and fatigue. The first tangible objective of the GENEQOL Consortium is to develop a list of potential biological pathways, genes and genetic variants involved in these quality-of-life outcomes, by reviewing current genetic knowledge. The second objective is to design a research agenda to investigate and validate those genes and genetic variants of patient-reported quality-of-life outcomes, by creating large datasets. During its first meeting, the Consortium has discussed draft summary documents addressing these questions for each patient-reported quality-of-life outcome. A summary of the primary pathways and robust findings of the genetic variants involved is presented here. The research agenda outlines possible research objectives and approaches to examine these and new quality-of-life domains. Intriguing questions arising from this endeavor are discussed. Insight into the genetic versus environmental components of patient-reported quality-of-life outcomes will ultimately allow us to explore new pathways for improving patient care. If we can identify patients who are susceptible to poor quality of life, we will be able to better target specific clinical interventions to enhance their quality of life and treatment outcomes.

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### **Surgery**

Deeb, D., X. H. Gao, H. Jiang, S. A. Dulchavsky and S. C. Gautam (2009). "Oleanane Triterpenoid CDDO-Me Inhibits Growth and Induces Apoptosis in Prostate Cancer Cells by Independently Targeting Pro-Survival Akt and mTOR." *Prostate* **69**(8): 851-860. [PDF Full-Text](#)

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**BACKGROUND.** Synthetic triterpenoids are potent anticancer agents, but their therapeutic efficacy or mechanism of action for prostate cancer has not been investigated. The goal of this study was to determine the antitumor activity and the mechanism of action of methyl-2-cyano-3,12-dioxooleana-1,9(11)-dien-28-oate (CDDO-Me), a oleanane-derived synthetic triterpenoid for human prostate cancer cells. **METHODS.** The antitumor activity of CDDO-Me for hormone-refractory PC-3 (AR(-)) and C4-2 (AR(+)) prostate cancer cell lines was determined by effects on cell growth and induction of apoptosis, identification of molecular targets, and therapeutic efficacy in vivo in PC-3 xenograft model. **RESULTS.** CDDO-Me inhibited the growth and induced apoptosis in PC-3 and C4-2 cells at extremely low concentrations. The antitumor activity of CDDO-Me was associated with the inhibition of p-Akt, mammalian target of rapamycin (mTOR), and nuclear factor kappa B (NF-kappa B) signaling proteins and their downstream targets such as p-Bad and p-Foxo3a (Akt); p-S6K1, p-eIF-4E and p-4E-BP1 (mTOR); and COX-2, VEGF and cyclin D1(NF-kappa B). Silencing of Akt sensitized the PC-3 cells to CDDO-Me, whereas overexpression of Akt induced resistance to CDDO-Me. Targeted silencing of Akt showed that Akt does not regulate mTOR activation in PC-3 cells, but targeted silencing of mTOR sensitized PC-3 cells to CDDO-Me mediated growth inhibition. Further, treatment with CDDO-Me inhibited the growth of PC-3 xenografts in nude mice. **CONCLUSIONS.** This study demonstrated potent antitumor activity of CDDO-Me against prostate cancer cells both in vitro and in vivo. Data also identified Akt and mTOR as molecular targets of CDDO-Me in prostate cancer cells. *Prostate* 69: 851-860, 2009. (c) 2009 Wiley-Liss, Inc.

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### **Surgery**

Gao, X., D. Deeb, Y. Liu, S. Gautam, S. A. Dulchavsky and S. C. Gautam (2009).

"Immunomodulatory activity of xanthohumol: inhibition of T cell proliferation, cell-mediated cytotoxicity and Th1 cytokine production through suppression of NF-kappaB."

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

Division of Surgical Research, Department of Surgery, Henry Ford Health System, Detroit, Michigan, USA.

Xanthohumol (XN), a prenylated chalcone present in hops (*Humulus lupulus* L.) and beer, exhibits anti-inflammatory, antioxidant and antiproliferative activity, but has not been studied for effects on T cell-mediated immune responses. Here we demonstrate that XN has profound immunosuppressive effects on T cell proliferation, development of IL-2 activated killer (LAK) cells, cytotoxic T lymphocytes (CTLs), and production

of Th1 cytokines (IL-2, IFN-gamma and TNF-alpha). The suppression of these cell-mediated immune responses by XN was at, least in part, due to the inhibition of nuclear factor kappa B (NF-kappaB) transcription factor through suppression of phosphorylation of I kappa B alpha, an inhibitor of NF-kappaB.

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## **Surgery**

Joseph, B., J. M. Morton, T. Hernandez-Boussard, I. Rubinfeld, C. Faraj and V. Velanovich (2009). "Relationship between hospital volume, system clinical resources, and mortality in pancreatic resection." *J Am Coll Surg* **208**(4): 520-7. [PDF Full-Text](#)

Division of General Surgery, Henry Ford Hospital, Detroit, MI 48202, USA.

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

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## **Surgery**

Kakkos, S. K., D. J. Reddy, A. D. Shepard, J. C. Lin, T. J. Nypaver and M. R. Weaver (2009). "Contemporary presentation and evolution of management of neck paragangliomas." *J Vasc Surg* **49**(6): 1365-73 e2. [PDF Full-Text](#)

Division of Vascular Surgery, Department of Surgery, Henry Ford Hospital, Detroit, MI, USA.

**BACKGROUND:** The aim of the present study was to review the contemporary presentation and evolution of management of neck paragangliomas. **METHODS:** Forty-one neck paragangliomas operated on in 36 patients over a 44 year period were included in the current report. The study period was divided into two parts, the first three decades (1964-1989), during which the current management techniques were evolved, and the last two decades (1990-2008). **RESULTS:** Patients presented with a palpable neck mass ( $n = 17$ ), cranial nerve (CN) palsy ( $n = 3$ ) or both ( $n = 6$ ), or the lesion was an incidental finding ( $n = 14$ ). The use of cross-section imaging modalities ( $n = 24$ ) increased from 35% during the first part of the study to 95% during the second part of the study ( $P < .001$ ). Preoperative embolization (introduced in 1979) was performed in 60% (median size 4.3 cm for embolized vs 3 cm [ $P = .02$ ], for non-embolized tumors). During the first study period, the frequency of Shamblin group II/III tumors was 95% compared with a frequency of 42% during the second study period ( $P < .001$ , odds ratio 25), median blood loss was 600 ml and 150 ml, respectively ( $P = .001$ ) and the transfusion rate was 44% and 5%, respectively ( $P = .008$ ). The incidence of temporary and permanent new CN deficits postoperatively was 22.5% and 10%, respectively, and was similar during the two study periods. Three tumors were malignant, based on lymph node involvement ( $n = 1$ ) or development of late metastases ( $n = 2$ ). **CONCLUSIONS:** In the modern era, neck paragangliomas can be managed with a low incidence of long-term

sequelae. Smaller, asymptomatic, and incidentally detected tumors are currently the most common presentation pattern.

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## **Surgery**

Koestner, A., M. R. Walters, C. Mattice, P. Manion and C. Seguin (2009). "Senior Lifestyles and Injury Prevention: Evaluating the Effectiveness of an Injury Prevention Program for Older Adults." J Trauma Nurs **16**(2): 87-92. [PDF Full-Text](#)

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The purpose of this multicenter, before-and-after observational study was to determine whether a short educational intervention was associated with improvement in self-reported safety behavior in older adults. We developed 4 original injury prevention presentations with companion testing materials: Motor Vehicle Safety, Fall Prevention, Pedestrian Safety, and Home Safety. Participants also completed pre-post Short Form Health Survey Instrument (SF-12) quality-of-life surveys. Of 414 participants, 226 completed follow-up testing and SF-12 surveys, for a 54.6% response rate. Those who completed either Pedestrian or Home Safety program showed no significant changes ( $P > .05$ ) in either test scores or SF-12, and they comprised 61.9% of the final sample. Participants in the Motor Vehicle Safety and Fall Prevention programs accounted for 38.1% of the final sample and did show significant improvements between pre-post test scores. Only Fall Prevention participants showed significant differences in pre-post SF-12 scores. In the Fall Prevention group, numerous SF-12 subscores from the initial survey were significantly inversely correlated with pretest scores, and improvements in some SF-12 subscores correlated with improvements in test scores. Findings from the Fall Prevention group suggest that seniors with quality-of-life limitations may be aware of their increased risk and more willing to make changes to enhance safety. Further study is needed because many questions regarding optimal approaches to injury prevention in the aging demographic remain unanswered.

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## **Surgery**

Lin, J. C., D. J. Reddy, D. Eun, M. Fumo and M. Menon (2009). "Robotic-Assisted Laparoscopic Dissection of the Infrarenal Aorta and Iliac Artery: A Technical Description and Early Results." Annals of Vascular Surgery **23**(3): 298-302. [PDF Full-Text](#)

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We report our initial experience with a novel robotic-assisted dissection of the infrarenal aorta and iliac arteries for the treatment of aortoiliac occlusive disease and abdominal aortoiliac aneurysm. Seven patients underwent the procedure using the da Vinci Surgical System. Transabdominal, retroperitoneal dissection of the aorta and iliac arteries was completed using the robotic system; then, a mini-laparotomy and hand-sewn aorta-to-graft anastomosis were performed. There was no mortality in this series of patients. This novel technique may overcome the difficulty of aortic dissection in a purely laparoscopic aortic surgery and serves as a bridging step toward totally robotic-assisted aortic surgery.

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## **Surgery**

Lonergan, I. and K. Moquin (2009). "Use of the VersaJet for pedicle deepithelialization during breast reduction surgery." *Aesthetic Plast Surg* 33(2): 250-3. [PDF Full-Text](#)

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**BACKGROUND:** Many modern techniques of breast reduction require that a pedicle of breast tissue be deepithelialized. The process of deepithelialization is both tedious and time consuming. Many techniques have been described to facilitate the process of deepithelialization in breast reduction, but none have replaced the gold standard of using the scalpel. This series details the authors' results using the VersaJet Hydrosurgery System for pedicle deepithelialization in breast reduction surgery. **METHODS:** In this study, 20 patients underwent inferior pedicle breast reduction using the VersaJet for pedicle deepithelialization between September 2006 and June 2007. The overall time required for pedicle deepithelialization using the VersaJet was compared with the average overall time required for deepithelialization using the scalpel. Intraoperative and postoperative complications were recorded. **RESULTS:** An overall time-savings of 10 to 25 min per case was noted using the VersaJet for pedicle deepithelialization rather than the scalpel. No intraoperative or postoperative complications were encountered due to use of the VersaJet for pedicle deepithelialization. **CONCLUSIONS:** The VersaJet is a safe and effective tool for pedicle deepithelialization in breast reduction surgery. The VersaJet significantly facilitates the process of pedicle deepithelialization and requires less time than use of the scalpel for the procedure.

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## **Urology**

Jhaveri, K., P. Chhabra, Y. M. Tan, R. Rao, G. Bartsch, M. Menon, A. Leung, A. Yadav, E. Te, E. D. Vaughan and K. Tewari (2009). "Evolution of the Robotic Continence Preservation Technique: An Anatomical Approach." *European Urology Supplements* 8(4): 383-383. [PDF Full-Text](#)

[Jhaveri, K.; Chhabra, P.; Tan, Y. M.; Rao, R.; Leung, A.; Yadav, A.; Te, E.; Vaughan, Jr. E. D.; Tewari, K.] Cornell Univ, Weill Med Coll, Dept Urol, New York, NY 10021 USA. [Bartsch, G.] Innsbruck Med Univ, Dept Urol, Innsbruck, Austria. [Menon, M.] Henry Ford Hlth Syst, Dept Urol, Detroit, MI USA.

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## **Urology**

Laungani, R. G., N. Seleno and A. M. Carlin (2009). "Effect of laparoscopic gastric bypass surgery on urinary incontinence in morbidly obese women." *Surgery for Obesity and Related Diseases* 5(3): 334-338. [Article Request Form](#)

[Laungani, Rajesh G.; Seleno, Nicole] Henry Ford Hlth Syst, Vattikuti Urol Inst, Detroit, MI USA. [Carlin, Arthur M.] Henry Ford Hosp, Div Gen Surg, Detroit, MI 48202 USA. Laungani, RG, Henry Ford Hlth Syst, Vattikuti Urol Inst, Detroit, MI USA.

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

within 3 months after LGB with as little as 30 lb of weight loss. Conclusion: UI is a common co-morbidity in the morbidly obese and was prevalent in two thirds of female patients presenting for bariatric Surgery evaluation. LGB with resultant weight loss significantly improved the UI symptoms and quality of life. (Surg Obes Relat Dis, 2009;5: 334-338.) (C) 2009 American Society for Metabolic and Bariatric Surgery. All rights reserved.

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### **Urology**

Menon, M. (2009). "Re: Finley et al.: Hypothermic Nerve-sparing Radical Prostatectomy: Rationale, Feasibility, and Effect on Early Continence. (Urology 2009;73:691-696)." Urology **73**(6): 1426-1427. [PDF Full-Text](#)

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### **Urology**

Patel, M. N., M. Bhandari, M. Menon and C. G. Rogers (2009). "Robotic-assisted partial nephrectomy." BJU Int **103**(9): 1296-311. [PDF Full-Text](#)

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