

## Henry Ford Health System Publication List October 2008

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

### **Biostatistics & Research Epidemiology**

Alexander, G. L., J. Calvi, M. Stopponi, J. McClure, S. Rolnick, G. Divine, V. Strecher and C. C. Johnson (2008). "Diet change for cancer prevention: Outcomes of the online menu choices intervention." *Annals of Behavioral Medicine* **35**: S76-S76. [PDF Full-Text](#)

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### **Biostatistics & Research Epidemiology**

Davis, R. E., J. Calvi, G. Alexander, J. Anderson, N. Zhang and K. Resnicow (2008). "Tailoring on Black identity: The eat for life trial." *Annals of Behavioral Medicine* **35**: S231-S231. [PDF Full-Text](#)

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### **Biostatistics & Research Epidemiology**

Joseph, C. L., S. L. Havstad, D. R. Ownby, E. Zoratti, E. L. Peterson, S. Stringer and C. C. Johnson (2008). "Gender differences in the association of overweight and asthma morbidity among urban adolescents with asthma." *Pediatr Allergy Immunol.* Epub Ahead of Print. [PDF Full-Text](#)

Henry Ford Health System, Department of Biostatistics & Research Epidemiology, Detroit, MI, USA.

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

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8:30am-7:30pm M-Th  
8:30am-5:00pm F

adolescents with asthma. Results have implications for clinical management as well as future research.

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### **Biostatistics & Research Epidemiology**

McClure, J., J. Richards, G. Alexander, C. Johnson, G. Divine, J. Calvi, C. Rolnick and M. Stopponi (2008). "It's not just smoking - Consider the other stuff, too: Risky health behaviors among smokers and nonsmokers."

Annals of Behavioral Medicine **35**: S194-S194. [PDF Full-Text](#)

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### **Biostatistics & Research Epidemiology**

Resnicow, K., R. E. Davis, G. Zhang, J. Konkell, V. J. Strecher, A. R. Shaikh, D. Tolsma, J. Calvi, G. Alexander, J. P. Anderson and C. Wiese (2008). "Tailoring a fruit and vegetable intervention on novel motivational constructs: Results of a randomized study." Annals of Behavioral Medicine **35**(2): 159-169. [PDF Full-Text](#)

**Background** Tailored health communications to date have been based on a rather narrow set of theoretical constructs. **Purpose** This study was designed to test whether tailoring a print-based fruit and vegetable (F & V) intervention on relatively novel constructs from self-determination theory (SDT) and motivational interviewing (MI) increases intervention impact, perceived relevance, and program satisfaction. The study also aimed to explore possible user characteristics that may moderate intervention response. **Methods** African American adults were recruited from two integrated health care delivery systems, one based in the Detroit Metro area and the other in the Atlanta Metro area, and then randomized to receive three tailored newsletters over 3 months. One set of newsletters was tailored only on demographic and social cognitive variables (control condition), whereas the other (experimental condition) was tailored on SDT and MI principles and strategies. The primary focus of the newsletters and the primary outcome for the study was fruit and vegetable intake assessed with two brief self-report measures. Preference for autonomy support was assessed at baseline with a single item: "In general, when it comes to my health I would rather an expert just tell me what I should do". Most between-group differences were examined using change scores. **Results** A total of 512 (31%) eligible participants, of 1,650 invited, were enrolled, of which 423 provided complete 3-month follow-up data. Considering the entire sample, there were no significant between-group differences in daily F & V intake at 3 month follow-up. Both groups showed similar increases of around one serving per day of F & V on the short form and half a serving per day on the long form. There were, however, significant interactions of intervention group with preference for autonomy-supportive communication as well as with age. Specifically, individuals in the experimental intervention who, at baseline, preferred an autonomy-supportive style of communication increased their F & V intake by 1.07 servings compared to 0.43 servings among controls. Among younger controls, there was a larger change in F & V intake, 0.59 servings, than their experimental group counterparts, 0.29 servings. Conversely, older experimental group participants showed a larger change in F & V, 1.09 servings, than older controls, 0.48. **Conclusion** Our study confirms the importance of assessing individual differences as potential moderators of tailored health interventions. For those who prefer an autonomy-supportive style of communication, tailoring on values and other motivational constructs can enhance message impact and perceived relevance.

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### **Biostatistics & Research Epidemiology**

Wells, K., M. Pladevall, E. L. Peterson, J. Campbell, M. Wang, D. E. Lanfear and L. K. Williams (2008). "Race-ethnic Differences in Factors

Associated with Inhaled Steroid Adherence Among Adult Asthmatics." [Am J Respir Crit Care Med](#). Epub Ahead of Print. [Article Request Form](#)

Department of Biostatistics and Research Epidemiology, Henry Ford Hospital, Detroit, Michigan, United States.

**RATIONALE:** Adherence to inhaled corticosteroid (ICS) medication is known to be low overall, but tends to be lower among African-American patients when compared with white patients. **OBJECTIVE:** To understand the factors which contribute to ICS adherence among African-American and white adults with asthma. **METHODS:** Eligible individuals had a prior diagnosis of asthma, one or more ICS prescriptions, and were members of a large health maintenance organization in southeast Michigan. Individuals were sent a survey which included questions about internal factors (e.g., patient beliefs, knowledge, and motivation) and external factors (e.g., socioeconomic status; barriers to care, social support; and stressors) potentially related to ICS adherence. Adherence was calculated using electronic prescription and fill data. Stepwise regression was used to identify factors associated with adherence before and after stratifying by race-ethnicity. **MEASUREMENTS AND MAIN RESULTS:** Surveys were returned by 1,006 (56.3%) of 1,787 eligible patients. Adjusting for internal factors, but not external factors, diminished the relationship between race-ethnicity and ICS adherence. Among African-American patients, readiness to take ICS medication was the only internal or external factor significantly associated with ICS adherence; it explained 5.6% of the variance in adherence. Among white patients, perceived ICS necessity, ICS knowledge, doctors being perceived as the source of asthma control, and readiness to take medication were the internal factors associated with ICS adherence; these accounted for 19.8% of the variance in adherence. **CONCLUSION:** Factors associated with ICS adherence appear to differ between African-American and white patients, suggesting that group-specific approaches are needed to improve adherence.

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### **Biostatistics & Research Epidemiology**

Xia, Y., H. Alhadlaq, N. Ramakrishnan, A. Bidthanapally, F. Badar and M. Lu (2008). "Molecular and morphological adaptations in compressed articular cartilage by polarized light microscopy and Fourier-transform infrared imaging." [J Structural Biology](#) **164**(1): 88-95. [Article Request Form](#)

Oakland University, Department of Physics, Rochester, MI 48309

Fifteen articular cartilage-bone specimens from one canine humeral joint were compressed in the strain range of 0-50%. The deformation of the extracellular matrices in cartilage was preserved and the same Received in revised form 12 June 2008 tissue sections were studied using Polarized light microscopy (PLM) and Fourier-transform infrared imaging (FTIRI). The PLM results show that the most significant changes in the apparent zone thickness due to 'reorganization' of the collagen fibrils based on the birefringence occur between 0% and 20% strain values, where the increase in the Superficial zone and decrease in the radial zone thicknesses are approximately linear with the applied strain. The FTIRI anisotropy results show that the two amide components Compression with bond direction perpendicular to the external compression retain anisotropy (amide 11 in the superficial zone and amide I in the radial zone). In contrast, the measured anisotropy from the two amide components with bond direction parallel to the external compression changes their anisotropy significantly amide 1 in the superficial zone and amide 11 in the radial zone). Statistical analysis shows that there is an excellent correlation ( $r= 0.98$ ) between the relative depth of the retardance in PLM and the relative depth of the amide 11 anisotropic cross-over. The changes in amide anisotropies in different histological zones are explained by the strain-dependent tipping angle of the amide bonds. These depth dependent adaptations to static loading in cartilage's morphological structure and chemical distribution could be useful in the future studies of the early diseased cartilage.

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### **Bone & Joint Center**

Wang, X., R. R. Zauel and D. P. Fyhrie (2008). "Postfailure modulus strongly affects microcracking and mechanical property change in human iliac cancellous bone: A study using a 2D nonlinear finite element method." J Biomechanics **41**(12): 2654-8. [PDF Full-Text](#)

Henry Ford Hospital, Detroit, MI 48202; Univ Calif Davis, Med Ctr, Lawrence J. Ellison Musculoskeletal Res Ctr, Sacramento, CA 95817

A two-dimensional (2D) finite element (FE) method was used to estimate the ability of bone tissue to sustain damage as a function of postfailure modulus. Briefly, 2D nonlinear compact-tension FE models were created from quantitative back-scattered electron images taken of human iliac crest bone specimens. The effects of different postfailure moduli on predicted microcrack propagation were examined. The 2D FE models were used as surrogates for real bone tissues. The crack number was larger in models with higher postfailure modulus, while mean crack length and area were smaller in these models. The rate of stiffness reduction was greater in the models with lower postfailure modulus. Hence, the current results supported the hypothesis that hard tissue postfailure properties have strong effects on bone microdamage morphology and the rate of change in apparent mechanical properties.

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### **Bone & Joint Center**

Yeni, Y. N., D. G. Kim, G. W. Divine, E. M. Johnson and D. D. Cody (2008). "Human cancellous bone from T12-L1 vertebrae has unique microstructural and trabecular shear stress properties." Bone. Epub Ahead of Print. [Article Request Form](#)

Section of Biomechanics, Bone and Joint Center, Henry Ford Hospital, 2799 West Grand Boulevard Detroit, MI, 48202, USA.

Increase of trabecular stress variability with loss of bone mass has been implicated as a mechanism for increased cancellous bone fragility with age and disease. In the current study, a previous observation that trabecular shear stress estimates vary along the human spine such that the cancellous tissue from the thoracic 12 (T12)-lumbar 1 (L1) junction experiences the highest trabecular stresses for a given load was tested as a formal hypothesis using multiple human spines. Thoracic 4, T5, T7, T9, T10, T12, L1, L2, L4 and L5 vertebrae from 10 human cadaver spines were examined. One specimen in the central anterior region was cored in the supero-inferior (SI) direction and another in the postero-lateral region was cored in the transverse (TR) direction from each vertebra. Micro-CT-based large-scale finite element models were constructed for each specimen and compression in the long axis of the cylindrical specimens was simulated. Cancellous bone modulus and the mean, the standard deviation, variability and amplification of trabecular von Mises stresses were computed. Bone volume fraction, trabecular number, trabecular thickness, trabecular separation, connectivity density and degree of anisotropy were calculated using 3D stereology. The results were analyzed using a mixed model in which spine level was modeled using a quadratic polynomial. The maximum of trabecular shear stress amplification and minimum of bone volume fraction were found in the cancellous tissue from the T12-L1 location when results from the samples of the same vertebra were averaged. When groups were separated, microstructure and trabecular stresses varied with spine level, extrema being at the T12-L1 levels, for the TR specimens only. SI/TR ratio of measured parameters also had quadratic relationships with spine level, the extrema being located at T12-L1 levels for most parameters. For microstructural parameters, these ratios approached to a value of one at the T12-L1 level, suggesting that T12-L1 vertebrae have more uniform cancellous tissue properties than other levels. The mean intercept length in the secondary principal direction of

trabecular orientation could account for the variation of all mechanical parameters with spine level. Our results support that cancellous tissue from T12-L1 levels is unique and may explain, in part, the higher incidence of vertebral fractures at these levels.

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### **Cardiology**

Bensimhon, D. R., E. S. Leifer, S. J. Ellis, J. L. Fleg, S. J. Keteyian, I. L. Pina, D. W. Kitzman, R. S. McKelvie, W. E. Kraus, D. E. Forman, A. J. Kao, D. J. Whellan, C. M. O'Connor and S. D. Russell (2008).

"Reproducibility of peak oxygen uptake and other cardiopulmonary exercise testing parameters in patients with heart failure (from the Heart Failure and A Controlled Trial Investigating Outcomes of exercise traiNing)." *American Journal of Cardiology* **102**(6): 712-717. [PDF Full-Text](#)

Peak oxygen uptake (pVo(2)) is an important parameter in assessing the functional capacity and prognosis of patients with heart failure. In heart failure trials, change in pVo(2) was often used to assess the effectiveness of an intervention. However, the within-subject variability of pVo(2) on serial testing may limit its usefulness. This study was designed to evaluate the within-subject variability of pVo(2) over 2 baseline cardiopulmonary exercise tests. As a substudy of the HF-ACTION trial, 398 subjects (73% men, 27% women; mean age 59 years) with heart failure and left ventricular ejection fraction  $\leq 35\%$  underwent 2 baseline cardiopulmonary exercise tests within 14 days. Mean pVo(2) was unchanged from test 1 to test 2 (15.16  $\pm$  4.97 vs 15.18  $\pm$  4.97 ml/kg/min;  $p = 0.78$ ). However, mean within-subject absolute change was 1.3 ml/kg/min (10th, 90th percentiles 0.1, 3.0), with 46% of subjects increasing and 48% decreasing on the second test. Other parameters, including the ventilation-to-carbon-dioxide production slope and Vo(2) at ventilatory threshold, also showed significant within-subject variation with minimal mean differences between tests. In conclusion, pVo(2) showed substantial within-subject variability in patients with heart failure and should be taken into account in clinical applications. However, on repeated baseline cardiopulmonary exercise tests, there appears to be no familiarization effect for Vo(2) in patients with HF. Therefore, in multicenter trials, there is no need to perform  $>1$  baseline cardiopulmonary exercise test. (C) 2008 Elsevier Inc. All rights reserved.

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### **Cardiology**

Clark, N. M., N. K. Janz, J. A. Dodge, L. Mosca, X. Lin, Q. Long, R. J. Little, J. R. C. Wheeler, S. Keteyian and J. Liang (2008). "The effect of patient choice of intervention on health outcomes." *Contemporary Clinical Trials* **29**(5): 679-686. [Article Request Form](#)

Background: Patient preference may influence intervention effects, but has not been extensively studied. Randomized controlled design (N= 1075) assessed outcomes when women (60 years+) were given a choice of two formats of a program to enhance heart disease management. Methods: Randomization to "no choice" or "choice" study arms. Further randomization of "no choice" to: 1) Group intervention program format, 2) Self-Directed program format, 3) Control Group. "Choice" arm selected their preferred program format. Baseline, four, twelve, and eighteen month follow-up data were collected. Two analyses: health outcomes for choice compared to being randomized; and preference effect on treatment efficacy. Results: Women who chose a format compared to being assigned a format had better psychosocial functioning at four months ( $p = 0.02$ ) and tended toward better physical functioning at twelve months ( $p = 0.07$ ). At eighteen months women who chose versus being assigned a format had more symptoms measured as: number ( $p = 0.004$ ), frequency ( $p = 0.006$ ) and bother ( $P = 0.004$ ). At four months women who preferred the Group format had better psychosocial functioning when assigned the Group format than when they were assigned the Self-Directed format ( $p = 0.03$ ). At eighteen months women preferring a Group format had more symptoms:

number ( $p=0.001$ ), frequency ( $p=0.001$ ), bother ( $p=0.001$ ) when assigned the Group format than when assigned the Self-Directed format. Conclusions: Choice and preference for the Group format each enhanced psychosocial and physical functioning up to one year. Despite the preference for Group format, over the longer term (eighteen months) cardiac symptoms were fewer when assigned the Self-Directed format. (C) 2008 Elsevier Inc. All rights reserved.

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### **Cardiology**

Czerska, B. (2008). "HF patients with preserved or reduced ejection fractions did not differ for survival or CV mortality at 5 years." Evid Based Med **13**(5): 153. [PDF Full-Text](#)

Henry Ford Hospital, Detroit, Michigan, USA.

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### **Cardiology**

Ebrahimian, T., P. Paradis, P. J. Pagano and E. L. Schiffrin (2008). "MAP kinase-activated protein kinase 2 mediates angiotensin II-induced oxidative stress: Regulation of NADPH oxidase subunits." Hypertension **52**(4): E120-E120. *Sladen has electronic subscription. Issue for this article not available online at the time of this publication.*

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### **Cardiology**

Greenberg, B., B. Czerska, R. M. Delgado, R. Bourge, M. R. Zile, M. Silver, M. Klapholz, E. Haeusslein, M. R. Mehra, P. Mather, W. T. Abraham, J. D. Neaton, B. S. Brown, I. C. Parker and M. A. Konstam (2008). "Effects of continuous aortic flow augmentation in patients with exacerbation of heart failure inadequately responsive to medical therapy - Results of the Multicenter Trial of the Orqis Medical Cancion System for the Enhanced Treatment of Heart Failure Unresponsive to Medical Therapy (MOMENTUM)." Circulation **118**(12): 1241-1249. [PDF Full-Text](#)

Background-Prior investigations suggest that superimposing continuous flow on aortic flow (continuous aortic flow augmentation) produces vasodilation, cardiac unloading, and improved cardiac performance. Methods and Results-We compared percutaneous continuous aortic flow augmentation (flow  $\leq 1.5$  L/min for up to 96 hours) plus medical therapy versus medical therapy alone by randomizing 168 patients (device,  $n = 109$ ; control,  $n = 59$ ) hospitalized with heart failure, reduced left ventricular ejection fraction and cardiac index, elevated pulmonary capillary wedge pressure, and renal impairment or substantial diuretic requirement despite intravenous inotropes/vasodilators. The primary composite efficacy end point included pulmonary capillary wedge pressure (72 to 96 hours) and days alive out of hospital off mechanical support over 35 days. The population's illness severity posed unique challenges. Enrollment ended early because of an inability to demonstrate significant benefit on the primary composite end point (device, 17.4%; control, 13.6%;  $P = 0.45$ ) in the face of excess device group bleeding. Pulmonary capillary wedge pressure decreased from  $28.8 \pm 6.3$  mm Hg (mean  $\pm$  SD) to  $24.9 \pm 7.2$  mm Hg (average, 72 to 96 hours) and  $28.9 \pm 7.1$  to  $26.5 \pm 6.2$  mm Hg in the device and control groups, respectively (between-group  $P = 0.074$ ). Cardiac index progressively increased in the device ( $2.05 \pm 0.53$  to  $2.44 \pm 0.52$  L  $\cdot$  min<sup>(-1)</sup>  $\cdot$  m<sup>(-2)</sup>) but not the control (between-group  $P < 0.0001$ ) group. Thirty-five-day Kansas City Cardiomyopathy Questionnaire Overall Summary scores increased by  $38.4 \pm 22.7$  and  $31.2 \pm 26.0$

points in the device and control groups (between-group  $P = 0.10$ ). Through 65 days, device-to-control hazard ratios were as follows: all-cause mortality, 1.05 (95% confidence interval, 0.60 to 1.82); death or heart failure hospitalization, 0.87 (95% confidence interval, 0.57 to 1.33); and heart failure hospitalization, 0.66 (95% confidence interval, 0.38 to 1.13). Major bleeds occurred in 16.5% in the device (7.3% treatment related) and 5.1% in the control ( $P = 0.05$ ) group. Conclusions-Continuous aortic flow augmentation improved cardiac performance, improving cardiac index and pulmonary capillary wedge pressure, but statistical significance for the primary efficacy end point was not attained. Hemodynamic and clinical observations provide direction toward additional studies to further investigate the clinical effects of this treatment.

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### **Cardiology**

Lanfeard, D. E. (2008). "Genetic variation in the natriuretic peptide system and heart failure." Heart Fail Rev. Epub Ahead of Print. [PDF Full-Text](#)

Henry Ford Heart and Vascular Institute, Section of Advanced Heart Failure and Cardiac Transplantation, Henry Ford Hospital, 2799 W. Grand Boulevard, K14, Detroit, MI, 48202, USA, [dlanfea1@hfhs.org](mailto:dlanfea1@hfhs.org).

Heart failure (HF) is a modern epidemic and is one of the few cardiovascular diseases which is increasing in prevalence. The growing importance of the Natriuretic Peptide (NP) system in HF is well recognized. Laboratory tests for B-type Natriuretic Peptide (BNP) have proven value as diagnostic and prognostic tools in HF and are now part of routine clinical care. Furthermore, recombinant atrial natriuretic peptide (ANP) (carperitide) and BNP (nesiritide) and are approved HF therapies in Japan and the US, respectively and additional natriuretic peptides (e.g., CNP, urodilatin, and designer NPs) are under investigation for use in HF. Common genetic sequence variants are increasingly being recognized as determinants of disease risk or drug response and may help explain a portion of the inter-individual variation in the human NP system. This review describes current knowledge of NP system genetic variation as it pertains to HF as well as ongoing studies and where the field is expected to progress in the near future. To briefly summarize, NP system genetic variants have been associated with alterations in gene expression, NP levels, and cardiovascular disease. The next step forward will include specific investigations into how this genetic variation can advance 'Personalized Medicine', such as whether they impact the utility of diagnostic BNP testing or effectiveness of therapeutic NP infusion. This is already in progress, with pharmacogenetic studies of nesiritide currently underway. We expect that within 5 years there should be a reasonable idea of whether NP system genetic variation will have important clinical implications.

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### **Cardiology**

Rastogi, S., V. G. Sharov, S. Mishra, R. C. Gupta, B. Blackburn, L. Belardinelli, W. C. Stanley and H. N. Sabbah (2008). "Ranolazine combined with enalapril or metoprolol prevents progressive LV dysfunction and remodeling in dogs with moderate heart failure." Am J Physiol Heart Circ Physiol **295**(5): H2149-55. [PDF Full-Text](#)

Cardiovascular Research, Henry Ford Hospital, 2799 West Grand Blvd., Detroit, MI 48202. [hsabbah1@hfhs.org](mailto:hsabbah1@hfhs.org).

Acute intravenous infusion of ranolazine (Ran), an anti-ischemic/antiangina drug, was previously shown to improve left ventricular (LV) ejection fraction (EF) without a concomitant increase in myocardial oxygen consumption in dogs with chronic heart failure (HF). This study examined the effects of treatment with Ran alone and in combination with metoprolol (Met) or enalapril (Ena) on LV function and remodeling in dogs with HF. Dogs ( $n = 28$ ) with microembolization-induced HF were randomized to 3

mo oral treatment with Ran alone [375 mg twice daily (bid); n = 7], Ran (375 mg bid) in combination with Met tartrate (25 mg bid; n = 7), Ran (375 mg bid) in combination with Ena (10 mg bid; n = 7), or placebo (PL; Ran vehicle bid; n = 7). Ventriculographic measurements of LV end-diastolic volume (EDV) and end-systolic volume (ESV) and LV EF were obtained before treatment and after 3 mo of treatment. In PL-treated dogs, EDV and ESV increased significantly. Ran alone prevented the increase in EDV and ESV seen in the PL group and significantly increased EF, albeit modestly, from 35 +/- 1% to 37 +/- 2%. When combined with either Ena or Met, Ran prevented the increase in EDV, significantly decreased ESV, and markedly increased EF compared with those of PL. EF increased from 35 +/- 1% to 40 +/- 1% with Ran + Ena and from 34 +/- 1% to 41 +/- 1% with Ran + Met. Ran alone or in combination with Ena or Met was also associated with beneficial effects at the cellular level on histomorphometric parameters such as hypertrophy, fibrosis, and capillary density as well as the expression for pathological hypertrophy and Ca(2+) cycling genes. In conclusion, Ran prevented progressive LV dysfunction and global and cellular myocardial remodeling, and Ran in combination with Ena or Met improved LV function beyond that observed with Ran alone.

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### **Cardiology**

Rosca, M. G., E. J. Vazquez, J. Kerner, W. Parland, M. P. Chandler, W. Stanley, H. N. Sabbah and C. L. Hoppel (2008). "Cardiac mitochondria in heart failure: decrease in respirasomes and oxidative phosphorylation." Cardiovascular Research **80**(1): 30-39. [PDF Full-Text](#)

Aims Mitochondrial dysfunction is a major factor in heart failure (HF). A pronounced variability of mitochondrial electron transport chain (ETC) defects is reported to occur in severe acquired cardiomyopathies without a consistent trend for depressed activity or expression. The aim of this study was to define the defect in the integrative function of cardiac mitochondria in coronary microembolization-induced HF. Methods and results Studies were performed in the canine coronary microembolization-induced HF model of moderate severity. Oxidative phosphorylation was assessed as the integrative function of mitochondria, using a comprehensive variety of substrates in order to investigate mitochondrial membrane transport, dehydrogenase activity and electron-transport coupled to ATP synthesis. The supramolecular organization of the mitochondrial ETC also was investigated by native gel electrophoresis. We found a dramatic decrease in ADP-stimulated respiration that was not relieved by an uncoupler. Moreover, the ADP/O ratio was normal, indicating no defect in the phosphorylation apparatus. The data point to a defect in oxidative phosphorylation within the ETC. However, the individual activities of ETC complexes were normal. The amount of the supercomplex consisting of complex I/complex III dimer/complex IV, the major form of respirasome considered essential for oxidative phosphorylation, was decreased. Conclusions We propose that the mitochondrial defect lies in the supermolecular assembly rather than in the individual components of the ETC.

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### **Cardiology**

Somkin, C. P., A. Altschuler, L. Ackerson, D. Tolsma, S. J. Rolnick, R. Yood, W. D. Weaver, A. Von Worley, M. Hornbrook, D. J. Magid and A. S. Go (2008). "Cardiology clinical trial participation in community-based healthcare systems: Obstacles and opportunities." Contemporary Clinical Trials **29**(5): 646-653. [Article Request Form](#)

Background: The objective of our study was to examine cardiologists' and organizational leaders' interest in clinical trial participation and perceived barriers and facilitators to participation within ten diverse non-profit healthcare delivery systems. Trials play a pivotal role in advancing knowledge about the safety and efficacy of cardiovascular interventions and tests. Although cardiovascular trials successfully enroll patients, recruitment challenges persist. Community-based health systems could be an important source of participants and investigators, but little is known about community cardiologists'

experiences with trials. Methods: We interviewed 25 cardiology and administrative leaders and mailed questionnaires to all 280 cardiologists at 10 U.S. healthcare organizations. Results: The survey received a 73% response rate. While 60% of respondents had not participated in any trials in the past year, nearly 75% wanted greater participation. Cardiologists reported positive attitudes toward trial participation; more than half agreed that trials were their first choice of therapy for patients, if available. Almost all leaders described their organizations as valuing research but not necessarily trials. Major barriers to participation were lack of physician time and insufficient skilled research nurses. Conclusions: Cardiologists have considerable interest in trial participation. Major obstacles to increased participation are lack of time and effective infrastructure to support trials. These results suggest that community-based health systems are a rich source for cardiovascular research but additional funding and infrastructure are needed to leverage this resource. (C) 2008 Elsevier Inc. All rights reserved.

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### **Cardiology**

Undrovinas, A. and V. A. Maltsev (2008). "Late Sodium Current is a New Therapeutic Target to Improve Contractility and Rhythm in Failing Heart." Cardiovasc Hematol Agents Med Chem **6**(4): 348-59. [PDF Full-Text](#)

Henry Ford Hospital, Cardiovascular Research, Education & Research Bldg. Room 4015, 2799 West Grand Boulevard, Detroit, MI 48202-2689, USA. [aundrov1@hfhs.org](mailto:aundrov1@hfhs.org).

Most cardiac Na(+) channels open transiently within milliseconds upon membrane depolarization and are responsible for the excitation propagation. However, some channels remain active during hundreds of milliseconds, carrying the so-called persistent or late Na(+) current (I(NaL)) throughout the action potential plateau. I(NaL) is produced by special gating modes of the cardiac-specific Na(+) channel isoform. Experimental data accumulated over the past decade show the emerging importance of this late current component for the function of both normal and especially failing myocardium, where I(NaL) is reportedly increased. Na(+) channels represent a multi-protein complex and its activity is determined not only by the pore-forming alpha subunit but also by its auxiliary beta subunits, cytoskeleton, and by Ca(2+) signaling and trafficking proteins. Remodeling of this protein complex and intracellular signaling pathways may lead to alterations of I(NaL) in pathological conditions. Increased I(NaL) and the corresponding Na(+) influx in failing myocardium contribute to abnormal repolarization and an increased cell Ca(2+) load. Interventions designed to correct I(NaL) rescue normal repolarization and improve Ca(2+) handling and contractility of the failing cardiomyocytes. New therapeutic strategies to target both arrhythmias and deficient contractility in HF may not be limited to the selective inhibition of I(NaL) but also include multiple indirect, modulatory (e.g. Ca(2+)- or cytoskeleton- dependent) mechanisms of I(NaL) function.

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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 (2008). "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, Mich., 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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### **Center for Health Services Research**

Yang, J. J., E. G. Burchard, S. Choudhry, C. C. Johnson, D. R. Ownby, D. Favro, J. Chen, M. Akana, C. Ha, P. Y. Kwok, R. Krajenta, S. I. Havstad, C. L. Joseph, M. A. Seibold, M. D. Shriver and L. K. Williams (2008). "Differences in allergic sensitization by self-reported race and genetic ancestry." J Allerg Clin Immunol **122**(4): 820-7. [PDF Full-Text](#)

Background: Many allergic conditions occur more frequently in African American patients when compared with white patients; however, it is not known whether this represents genetic predisposition or disparate environmental exposures.

Objective: We sought to assess the relationship of self-reported race and genetic ancestry to allergic sensitization.

Methods: We included 601 women enrolled in a population-based cohort study whose self-reported race was African American or white. Genetic ancestry was estimated by using markers that differentiate West African and European ancestry. We assessed the relationship between allergic sensitization (defined as  $\geq 1$  allergen-specific IgE results) and both self-reported race and genetic ancestry. Regression models adjusted for sociodemographic variables, environmental exposures, and location of residence.

Results: The average proportion of West African ancestry in African American participants was 0.69, whereas the mean proportion of European ancestry in white participants was 0.79. Self-reported African American race was associated with allergic sensitization when compared with those who reported being white (adjusted odds ratio, 2.19; 95% CI, 1.22-3.93), even after adjusting for other variables. Genetic ancestry was not significantly associated with allergic sensitization after accounting for location of residence (adjusted odds ratio, 2.09 for urban vs suburban residence; 95% CI, 1.32-3.31).

Conclusion: Self-reported race and location of residence appeared to be more important predictors of allergic sensitization when compared with genetic ancestry, suggesting that the disparity in allergic sensitization by race might be primarily a result of environmental factors rather than genetic differences.

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

Williams, G. C., H. Patrick, C. P. Niemiec and M. Pladevall (2008). "Self-determination theory and medication adherence: Toward reducing the health risks of diabetes." Annals of Behavioral Medicine **35**: S14-S14. [PDF Full-Text](#)

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## **Dermatology**

Eide, M. J., M. A. Weinstock and M. A. Clark (2008). "The association of physician-specialty density and melanoma prognosis in the United States, 1988 to 1993." J Am Acad Dermatol. EPub Ahead of Print. [PDF Full-Text](#)

Department of Community Health, Center for Gerontology Providence, Rhode Island; Healthcare Research, Brown University, Providence, Rhode Island; Department of Dermatology, Henry Ford Hospital, Detroit, Michigan.

BACKGROUND: Studies suggest physician workforce may influence cancer outcomes. OBJECTIVE: We sought to quantify the effect of physician-specialty density on melanoma prognosis. METHODS: Data from 17,702 melanoma cases reported to the Surveillance, Epidemiology, and End Results program from 1988 to 1993 were merged with sociodemographic data (1990 US Census) and dermatologist, family practitioner, and internist density data (Area Resource File). Linear and logistic regression analyses were used to model prognosis (melanoma mortality to incidence ratio). RESULTS: A higher density of dermatologists was associated with better prognosis (lower mortality to incidence ratio) ( $\beta = -50 \times 10^{-4}$ ; SE  $8 \times 10^{-4}$ ). Internist density was also a significant predictor of better prognosis whereas increased family practitioner density was associated with worse prognosis. Controlling for sociodemographics, physician density remained a significant predictor of the mortality to incidence ratio. LIMITATIONS: Socioeconomic factors were estimated. Physician density was examined by county. CONCLUSION: Controlling for sociodemographic factors, physician-specialty density predicted melanoma prognosis. This suggests that specialist health care availability may affect melanoma outcomes.

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## **Emergency Medicine**

Birkhahn, R. H., A. L. Blomkalns, H. A. Klausner, R. M. Nowak, A. S. Raja, R. L. Summers, J. E. Weber, W. M. Briggs, A. Arkun and D. Diercks (2008). "Academic emergency medicine faculty and industry relationships." Academic Emergency Medicine 15(9): 819-824. [PDF Full-Text](#)

Objectives: The authors surveyed the membership of the Society for Academic Emergency Medicine (SAEM) about their associations with industry and predictors of those associations. Methods: A national Web-based survey inviting faculty from the active member list of SAEM was conducted. Follow-up requests for participation were sent weekly for 3 weeks. Information was collected on respondents' personal and practice characteristics, industry interactions, and personal opinions regarding these interactions. Raw response rates were reported and a logistic regression was used to generate descriptive statistics. Results: Responses were received from 430 members, representing 14% of the 3,183 active members. Respondents were 83% male and 86% white, with 96% holding an MD degree (24% with an additional postdoctoral degree). Most were at the assistant (37%) or associate (25%) professor rank, with 51% holding at least one leadership position. Most respondents (82%) reported some type of industry interaction, most commonly the acceptance of food or beverages (67%). Respondents at the associate professor rank or higher were more likely to receive payments from industry (51% vs. 22%, odds ratio [OR] = 3.7). Conclusions: This survey suggests that interactions between industry and academic EM faculty are common and increase with academic rank, but not with years in practice or leadership influence. The number and type of interactions are consistent with those reported by a national sampling of other physician specialties.

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## **Emergency Medicine**

Kanjanauthai, S., T. Kanluen and C. Ray (2008). "Pulmonary artery sarcoma masquerading as saddle pulmonary embolism." Heart Lung and Circulation **17**(5): 417-419. [Article Request Form](#)

Pulmonary artery sarcoma is a highly malignant tumour. Therefore, making the diagnosis is very important. We describe a case which presented with dyspnea on exertion and was initially diagnosed as saddle pulmonary embolism per CT thorax with contrast. Despite adequate anticoagulation, symptoms still progressed. Follow-up CT thorax showed an extension of the presumed filling defect or clots into the left main pulmonary artery with new lung nodules. This prompted suspicion that this may not be a pulmonary embolism. Biopsy of the lung nodule revealed high grade soft tissue sarcoma with primary source from the pulmonary artery. Our case highlights that pulmonary artery sarcoma should always be included in the differential diagnosis of pulmonary embolism especially, if symptoms still progress while on adequate anti coagulation, or any pulmonary nodules develop on follow-up exam.

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### **Emergency Medicine**

Morris, D. C. (2008). "Vasopressors in cardiopulmonary resuscitation." N Engl J Med **359**(15): 1624. [PDF Full-Text](#)

Henry Ford Health System, Detroit, MI 48202, [dmorris4@hfhs.org](mailto:dmorris4@hfhs.org)

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### **Emergency Medicine**

Sasson, C., A. J. Hegg, M. Macy, A. Park, A. Kellermann and B. McNally (2008). "Prehospital termination of resuscitation in cases of refractory out-of-hospital cardiac arrest." JAMA **300**(12): 1432-8. [PDF Full-Text](#)

Context Identifying patients in the out- of- hospital setting who have no realistic hope of surviving an out- of- hospital cardiac arrest could enhance utilization of scarce health care resources. Objective To validate 2 out- of- hospital termination- of- resuscitation rules developed by the Ontario Prehospital Life Support ( OPALS) study group, one for use by responders providing basic life support ( BLS) and the other for those providing advanced life support ( ALS). Design, Setting, and Patients Retrospective cohort study using surveillance data prospectively submitted by emergency medical systems and hospitals in 8 US cities to the Cardiac Arrest Registry to Enhance Survival ( CARES) between October 1, 2005, and April 30, 2008. Case patients were 7235 adults with out- of- hospital cardiac arrest; of these, 5505 met inclusion criteria. Main Outcome Measures Specificity and positive predictive value of each termination-of-resuscitation rule for identifying patients who likely will not survive to hospital discharge. Results The overall rate of survival to hospital discharge was 7.1% ( n= 392). Of 2592 patients ( 47.1%) who met BLS criteria for termination of resuscitation efforts, only 5( 0.2%) patients survived to hospital discharge. Of 1192 patients ( 21.7%) who met ALS criteria, none survived to hospital discharge. The BLS rule had a specificity of 0.987( 95% confidence interval [ CI], 0.970- 0.996) and a positive predictive value of 0.998( 95% CI, 0.996- 0.999) for predicting lack of survival. The ALS rule had a specificity of 1.000( 95% CI, 0.991- 1.000) and positive predictive value of 1.000( 95% CI, 0.997- 1.000) for predicting lack of survival. Conclusion In this validation study, the BLS and ALS termination- of- resuscitation rules performed well in identifying patients with out- of- hospital cardiac arrest who have little or no chance of survival.

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### **Eye Care Services**

Guo, A. M., J. Sheng, G. M. Scicli, A. S. Arbab, N. L. Lehman, P. A. Edwards, J. R. Falck, R. J. Roman and A. G. Scicli (2008). "Expression of

CYP4A1 in U251 human glioma cell induces hyperproliferative phenotype in vitro and rapidly growing tumors in vivo." J Pharmacol Exp Ther **327**(1): 10-9. [PDF Full-Text](#)

Henry Ford Hospital, Detroit, Michigan 48202, USA. [mguo1@hfhs.org](mailto:mguo1@hfhs.org)

Exogenous 20-hydroxyeicosatetraenoic acid (20-HETE) increases the growth of human glioma cells in vitro. However, glioma cells in culture show negligible 20-HETE synthesis. We examined whether inducing the expression of a 20-HETE synthase in a human glioma U251 cell line would increase proliferation. U251 cells transfected with CYP4A1 cDNA (termed U251 O) increased the formation of 20-HETE from less than 1 to over 60 pmol/min/mg proteins and increased their proliferation rate by 2-fold ( $p < 0.01$ ). Compared with control U251, U251 O cells were rounded, smaller, showed a disorganized cytoskeleton, exhibited reduced vinculin staining, and were easily detached from the growing surface. They showed a marked increase in dihydroethidium staining, suggesting increased oxidative stress. The expression of phosphorylated extracellular signal-regulated kinase 1/2, cyclin D1/2, and vascular endothelial growth factor was markedly elevated in U251 O. The hyperproliferative and signaling effects seen in U251 O cells are abolished by selective CYP4A inhibition of 20-HETE formation with HET0016 [N-hydroxy-N'-(4-butyl-2-methylphenyl)-formamidine], by small interfering RNA against the enzyme, and by the putative 20-HETE antagonist, 20-hydroxyeicosa-5(Z),14(Z)-dienoic acid. In vivo, implantation of U251O cells in the brain of nude rats resulted in a approximately 10-fold larger tumor volume (10 days postimplantation) compared with animals receiving mock-transfected U251 cells. These data show that elevations in 20-HETE synthesis in U251 cells lead to an increased growth both in vitro and in vivo. This suggests that 20-HETE may have proto-oncogenic properties in U251 human gliomas. Further studies are needed to determine whether 20-HETE plays a role promoting growth of some human gliomas.

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### **Eye Care Services**

O'Donnell, C. and M. E. Daniel (2008). "Aging successfully with vision loss: Engaging in creative occupations." OT Pract **13**(12): 14-18. [Article Request Form](#)

Henry Ford Visual Rehabilitation and Research Center.

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### **Eye Care Services**

Trick, G. L., P. A. Edwards, U. Desai, P. E. Morton, Z. Latif and B. A. Berkowitz (2008). "MRI retinovascular studies in humans: research in patients with diabetes." NMR Biomed **21**(9): 1003-12. [Article Request Form](#)

Department of Ophthalmology, Henry Ford Health System, Detroit, MI, USA.

PURPOSE: To review existing applications of MRI for detecting blood-retinal barrier (BRB) damage and retinal oxygenation response abnormalities in patients with diabetes and highlight new information available from such applications. METHODS: BRB studies were accomplished using dynamic contrast-enhanced MRI, and the retinal oxygenation response studies were accomplished by monitoring changes in the MRI signal associated with hyperoxic provocation. Participants were patients with diabetes and macular edema, with either no detectable or mild to moderate background retinopathy, as well as non-diabetic individuals of similar age (controls). Single-slice FLASH images were obtained using a Siemens Sonata, 1.5 T together with a Siemens 'Loop Small' surface coil fixed in

place over the eye. Time-dependent changes in image contrast in the pre-retinal vitreous were quantified, and differences between patients and controls were assessed statistically. RESULTS: The BRB breakdown studies showed a significant difference in the temporal evolution of the MRI signal enhancement post-contrast injection between the controls and the patients with diabetic macular edema. The retinal oxygenation studies revealed a supernormal oxygenation response in the pre-retinal vitreous in patients with diabetes who had no evidence of retinopathy, as well as in patients with background diabetic retinopathy. A nasal-temporal asymmetry in the evolution of retinal oxygenation response was found in patients with diabetes that was not present in healthy subjects. CONCLUSIONS: These studies show that subtle differences in retinovascular function between patients with diabetes and non-diabetic individuals, including changes that occur in advance of the clinical appearance of diabetic retinopathy, can be detected with MRI. These results, together with previous extensive preclinical data, establish MRI as a powerful non-invasive method for measuring spatial and temporal changes in the same key retinovascular metrics in both animals and humans. Wide application of these techniques for diagnosis and evaluation of treatment efficacy in a variety of human retinopathies, including diabetic retinopathy, is expected. Copyright (c) 2008 John Wiley & Sons, Ltd.

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### **Gastroenterology**

Asfandiyar, S., A. Silverman and S. Gordon (2008). "Celiac disease should be considered in patients with cryptogenic cirrhosis." [American Journal of Gastroenterology](#) **103**(Suppl S): S326-S327. [PDF Full-Text](#)

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### **Gastroenterology**

Bhan, A., E. Castillo and A. Ormsby (2008). "Microscopic colitis: a retrospective analysis of clinical characteristics, association with autoimmune disorders, and response to therapy." [Am J Gastroenterol](#) **103**(Suppl S): S182-S183. [PDF Full-Text](#)

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### **Gastroenterology**

Khan, F., T. Al-Hassani and A. Nawras (2008). "Collagenous gastritis: An unusual cause of profound anemia in adolescents." [Am J Gastroenterol](#) **103**(Suppl S): S54. [PDF Full-Text](#)

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### **Gastroenterology**

Krishnan, P., H. Singh and S. Batra (2008). "A case report of villous adenoma of the terminal ileum masquerading as Crohn's disease." [Am J Gastroenterol](#) **103**(Suppl S): S298-9. [PDF Full-Text](#)

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### **Gastroenterology**

Prazak, J., R. Sabbagh and G. Olds (2008). "Long-term follow-up of patients with dilated common bile duct (CBD) and negative endoscopic ultrasonography (EUS) - a single-center experience." [Am J Gastroenterol](#) **103**(Suppl S): S61. [PDF Full-Text](#)

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**Hematology, Medical Oncology and Josephine Ford Cancer Center**  
Wade, C. H., C. M. McBride, S. H. Alford, A. D. Baxevanis, R. Reid, E. B. Larson and L. C. Brody (2008). "When genetic susceptibility testing is offered for multiple common health conditions, who is interested?" Annals of Behavioral Medicine **35**: S19-S19. [PDF Full-Text](#)

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**Hematology, Oncology & Josephine Ford Cancer Center**  
Lo, A. C., C. G. Kleer, M. Banerjee, S. Omar, H. Khaled, S. Eissa, A. Hablas, J. A. Douglas, S. H. Alford, S. D. Merajver and A. S. Soliman (2008). "Molecular epidemiologic features of inflammatory breast cancer: a comparison between Egyptian and US patients." Breast Cancer Research and Treatment **112**(1): 141-147. [PDF Full-Text](#)

**Background** Inflammatory breast cancer (IBC) is a lethal form of breast cancer with unknown etiology. A higher frequency of IBC and a more aggressive IBC phenotype was reported in Egypt than in the United States. This difference in disease frequency and presentation might be related to molecular epidemiologic factors. **Methods** We used tumor blocks and demographic, epidemiologic, and clinical data of 48 IBC patients from Egypt and 12 patients from the United States. We counted tumor emboli in tumors before and after immunohistochemical staining with lymphatic vessel endothelial receptor-1 (LYVE-1), and measured the expression of RhoC GTPase protein in the two groups. **Results** Erythema, edema, and peau d'orange were found in 77% of the Egyptian patients as compared with 29% found in the US patients ( $P = 0.02$ ). The number of tumor emboli was significantly higher in tumors from Egypt (mean  $\pm$  SD, 14.1  $\pm$  14.0) than in the tumors from the United States (5.0  $\pm$  4.0,  $P = 0.01$ ). The number of tumor emboli in LYVE-1 positive vessels was higher in tumors from Egypt (3.5  $\pm$  2.8) than tumors from the United States (1.6  $\pm$  0.5,  $P = 0.15$ ). We detected a high level of RhoC in 87% of the tumors from Egypt and 14% of the tumors from the United States ( $P = 0.0003$ ). **Conclusion** Patients from Egypt have a more aggressive form of IBC than those in the United States. Our analysis of IBC patients shows that distinct molecular phenotypes can be found when these two study populations are compared. Future studies should explore the epidemiologic and environmental exposures and the genetic factors that might lead to the different clinical and molecular features of IBC in patients from these two countries.

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**Hypertension & Vascular Research**  
Herrera, M. and J. L. Garvin (2008). "Angiotensin II stimulates NOS 3 phosphorylation via Akt in the thick ascending limb." Hypertension **52**(4): E70-E70. *Sladen has electronic subscription. Issue for this article not available online at the time of this publication.*

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**Hypertension & Vascular Research**  
Li, X. C., Y. Shao, X. G. Dai and J. L. Zhuo (2008). "Expression of AT(1) receptor and NHE-3 mRNAs and proteins is differentially regulated in proximal tubules of Ang II-induced hypertensive rats." Hypertension **52**(4): E57-E57. *Sladen has electronic subscription. Issue for this article not available online at the time of this publication.*

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**Hypertension & Vascular Research**

Li, X. C. and J. L. Zhuo (2008). "Roles of clathrin light chains and microtubule-associated proteins in AT(1) receptor-mediated ang II endocytosis and NHE-3 expression in rabbit proximal tubule cells." *Hypertension* **52**(4): E41-E41. *Sladen has electronic subscription. Issue for this article not available online at the time of this publication.*

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### **Hypertension & Vascular Research**

Liao, T. D., X. P. Yang, N. E. Rhaleb and O. A. Carretero (2008). "Ac-SDKP attenuates renal injury and fibrosis in rats with subtotal renal ablation." *Hypertension* **52**(4): E114-E114. *Sladen has electronic subscription. Issue for this article not available online at the time of this publication.*

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### **Hypertension & Vascular Research**

Lin, C. X., N. E. Rhaleb, X. P. Yang, T. D. Liao, M. A. D'Ambrosio and O. A. Carretero (2008). "Prevention of aortic fibrosis by N-acetyl-seryl-aspartyl-lysyl-proline in angiotensin II-induced hypertension." *Am J Physiol Heart Circ Physiol* **295**(3): H1253-H1261. [PDF Full-Text](#)

Hypertension and Vascular Research Div., Henry Ford Hospital, 2799 West Grand Blvd., Detroit, MI 48202-2689, USA.

Fibrosis is an important component of large conduit artery disease in hypertension. The endogenous tetrapeptide N-acetyl-seryl-aspartyl-lysyl-proline (Ac-SDKP) has anti-inflammatory and antifibrotic effects in the heart and kidney. However, it is not known whether Ac-SDKP has an anti-inflammatory and antifibrotic effect on conduit arteries such as the aorta. We hypothesize that in ANG II-induced hypertension Ac-SDKP prevents aortic fibrosis and that this effect is associated with decreased protein kinase C (PKC) activation, leading to reduced oxidative stress and inflammation and a decrease in the profibrotic cytokine transforming growth factor-beta1 (TGF-beta1) and phosphorylation of its second messenger Smad2. To test this hypothesis we used rats with ANG II-induced hypertension and treated them with either vehicle or Ac-SDKP. In this hypertensive model we found an increased collagen deposition and collagen type I and III mRNA expression in the aorta. These changes were associated with increased PKC activation, oxidative stress, intercellular adhesion molecule (ICAM)-1 mRNA expression, and macrophage infiltration. TGF-beta1 expression and Smad2 phosphorylation also increased. Ac-SDKP prevented these effects without decreasing blood pressure or aortic hypertrophy. Ac-SDKP also enhanced expression of inhibitory Smad7. These data indicate that in ANG II-induced hypertension Ac-SDKP has an aortic antifibrotic effect. This effect may be due in part to inhibition of PKC activation, which in turn could reduce oxidative stress, ICAM-1 expression, and macrophage infiltration. Part of the effect of Ac-SDKP could also be due to reduced expression of the profibrotic cytokine TGF-beta1 and inhibition of Smad2 phosphorylation.

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### **Hypertension & Vascular Research**

Ramseyer, V. D. and J. L. Garvin (2008). "Angiotensin II decreases NO synthase type 3 expression via reactive oxygen species in medullary thick ascending limbs." *Hypertension* **52**(4): E69-E69. *Sladen has electronic subscription. Issue for this article not available online at the time of this publication.*

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### **Hypertension & Vascular Research**

Ren, Y. L., M. A. D'Ambrosio, H. Wang, R. S. Liu, J. L. Garvin and O. A. Carretero (2008). "Heme oxygenase metabolites regulate tubuloglomerular feedback." Am J Physiology-Renal Physiology **295**(4): F1207-12. [PDF Full-Text](#)

Tubuloglomerular feedback (TGF) is the mechanism by which the macula densa (MD) senses increases in luminal NaCl concentration and sends a signal to constrict the afferent arteriole (Af-Art). The kidney expresses constitutively heme oxygenase-2 (HO-2) and low levels of HO-1. HOs release carbon monoxide (CO), biliverdin, and free iron. We hypothesized that renal HOs inhibit TGF via release of CO and biliverdin. Rabbit Af-Arts and attached MD were simultaneously microperfused in vitro. The TGF response was determined by measuring Af-Art diameter before and after increasing NaCl in the MD perfusate. When HO activity was inhibited by adding stannous mesoporphyrin (SnMP) to the MD perfusate, the TGF response increased from 2.1 +/- 0.2 to 4.1 +/- 0.4 +/-  $\mu$  m (P = 0.003, control vs. SnMP, n = 7). When a CO-releasing molecule, (CORM-3; 50  $\mu$  M), was added to the MD perfusate, the TGF response decreased by 41%, from 3.6 +/- 0.3 to 2.1 +/- 0.2  $\mu$  m (P < 0.001, control vs. CORM-3, n = 12). When CORM-3, at 100  $\mu$  M was added to the perfusate, it completely blocked the TGF response, from 4.2 +/- 0.4 to -0.2 +/- 0.3 +/-  $\mu$  m (P < 0.001, control vs. CORM-3, n = 6). When biliverdin was added to the perfusate, the TGF response decreased by 79%, from 3.4 +/- 0.3 to 0.7 +/- 0.4  $\mu$  m (P = 0.001, control vs. biliverdin, n = 6). The effects of SnMP and CORM-3 were not blocked by inhibition of nitric oxide synthase. We concluded that renal HO inhibits TGF probably via release of CO and biliverdin. HO regulation of TGF is a novel mechanism that could lead to a better understanding of the control of renal microcirculation and function.

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### **Hypertension & Vascular Research**

Silva, G. B. and J. L. Garvin (2008). "Reduced osmolality stimulates ATP release in the thick ascending limb by activating TRPV4." Hypertension **52**(4): E35-E35. *Sladen has electronic subscription. Issue for this article not available online at the time of this publication.*

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### **Hypertension & Vascular Research**

Wang, H., J. L. Garvin, Y. L. Ren, R. S. Liu and O. A. Carretero (2008). "Heme oxygenase metabolites regulate tubuloglomerular feedback in vivo." Am J Physiol Renal Physiol **295**(4): F1207-12. [PDF Full-Text](#)

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### **Hypertension & Vascular Surgery**

Ortiz-Capisano, C., P. A. Ortiz and W. H. Beierwaltes (2008). "Calcium-dependent phosphodiesterase-1C mediates renin release from isolated juxtaglomerular cells." Hypertension **52**(4): E68-E68. *Sladen has electronic subscription. Issue for this article not available online at the time of this publication.*

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### **Infectious Diseases**

Singh, N., O. Lortholary, F. Dromer, B. D. Alexander, K. L. Gupta, G. T. John, R. del Busto, G. B. Klintmalm, J. Somani, G. M. Lyon, K. Pursell, V. Stosor, P. Munoz, A. P. Limaye, A. C. Kalil, T. L. Pruett, J. Garcia-Diaz, A. Humar, S. Houston, A. A. House, D. Wray, S. Orloff, L. A. Dowdy, R. A. Fisher, J. Heitman, M. M. Wagener and S. Husain (2008). "Central nervous system cryptococcosis in solid organ transplant recipients: Clinical relevance of abnormal neuroimaging findings." Transplantation **86**(5): 647-651. [PDF Full-Text](#)

Background. Prognostic implications of cryptococcal antigen and outcomes associated with central nervous system (CNS) cryptococcal lesions in solid organ transplant recipients have not been fully defined. Methods. Patients were derived from a cohort of 122 solid organ transplant recipients with cryptococcosis in a multicenter study from 1999 to 2006. Results. Central nervous system cryptococcosis was documented in 61 patients. Serum or cerebral spinal fluid antigen titers did not correlate with mortality at 90 days or cerebral spinal fluid sterilization at 2 weeks. Central nervous system lesions were identified in 16 patients and included leptomenigeal lesions in eight, parenchymal lesions in six, and hydrocephalus in two. Overall, 13/16 CNS lesions were present at the time of diagnosis. One parenchymal and two hydrocephalus lesions, however, developed after diagnosis and fulfilled the criteria for immune reconstitution syndrome. Cerebral spinal fluid antigen titers were higher with meningeal versus parenchymal lesions, and hydrocephalus (P = 0.015). Mortality was 50% (3/6) for patients with parenchymal, 12.5% (1/8) for those with leptomenigeal, and 0/3 for patients with hydrocephalus. Mortality was 31% (4/13) for patients with CNS lesions at baseline and 0/3 in those with new onset lesions. Conclusions. Despite a higher antigen titer with meningeal lesions, outcomes tended to be worse with parenchymal compared with meningeal lesions or hydrocephalus. New onset CNS lesions may represent immune reconstitution syndrome and seemed to be associated with better outcome.

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### **Internal Medicine**

Clark, B. R., N. Engene, M. E. Teasdale, D. C. ORowley, T. Matainaho, F. A. Valeriote and W. H. Gerwick (2008). "Natural products chemistry and taxonomy of the marine cyanobacterium *Blennothrix cantharidosmum*." J Natural Products **71**(9): 1530-7. [Article Request Form](#)

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### **Internal Medicine**

Ponnezhan, V., H. Singh and O. Alaradi (2008). "The rate of post ERCP pancreatitis in liver transplant patients compared to non transplant patients, a single center experience." Am J Gastroenterol **103**(Suppl S): S84. [PDF Full-Text](#)

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### **Internal Medicine**

Sabbagh, R., P. Krishnan, K. Brown, D. Moonka and M. A. Sherbondy (2008). "How does the recipient's pre-transplant medical condition affect steatosis in the transplanted liver?" Am J Gastroenterol **103**(Suppl S): S148. [PDF Full-Text](#)

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### **Internal Medicine**

Spyropoulos, A. C., A. G. G. Turpie, A. S. Dunn, S. Kaatz, J. Douketis, A. Jacobson and H. Petersen (2008). "Perioperative bridging therapy with unfractionated heparin or low-molecular-weight heparin in patients with mechanical prosthetic heart valves on long-term oral anticoagulants (from the REGIMEN registry)." American Journal of Cardiology **102**(7): 883-889. [PDF Full-Text](#)

Patients with mechanical prosthetic heart valves require long-term oral anticoagulant therapy (OAT). During the temporary interruption of OAT, bridging anticoagulant therapy with unfractionated heparin (UFH) or low-molecular-weight heparin (LMWH) is recommended. This prespecified subgroup analysis from REGIMEN-a large, prospective, multicenter registry-compared UFH (n = 73) and LMWH (n = 172) as bridging anticoagulation in patients with mechanical heart valves on long-term OAT. Patient demographics and co-morbidities were generally similar between groups. There were more bileaflet valves in the LMWH group (67.4% vs 43.8%, p = 0.0005), but no differences in valve positions between groups. The LMWH group was less likely to undergo major surgery (33.7% vs 58.9%, p = 0.0002) and cardiothoracic surgery (7.6% vs 19.2%, p = 0.008), and to receive intraprocedural anticoagulants or thrombolytics (4.1% vs 13.7%, p = 0.007). Major adverse event rates (5.5% vs 10.3%, p = 0.23) and major bleeds (4.2% vs 8.8%, p = 0.17) were similar in the LMWH and UFH groups, respectively; 1 arterial thromboembolic event occurred in each group. More LMWH-bridged patients were treated as outpatients or discharged from the hospital in <24 hours (68.6% vs 6.8%, p <0.0001). Multivariate logistic analysis found no significant differences in major bleeds and major composite adverse events when adjusting for cardiothoracic or major surgery between groups. In conclusion, for patients with mechanical prosthetic heart valves on long-term OAT, mostly outpatient-based LMWH bridging therapy appears to be feasible for selected procedures, is as safe as UFH, and is associated with a low arterial thromboembolic rate. (C) 2008 Elsevier Inc. All rights reserved.

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### **Nephrology**

Besarab, A. (2008). "Resolved: Fistulas are preferred to grafts as initial vascular access for dialysis. Pro." J Am Soc Nephrol **19**(9): 1629-31. [PDF Full-Text](#)

Division of Nephrology and Hypertension, Department of Medicine, Henry Ford Hospital, Detroit, MI 48301, USA. [abesara1@hfhs.org](mailto:abesara1@hfhs.org)

There is growing concern that the Fistula First Initiative, KDOQI guidelines, and subsequent pressure from the Centers for Medicare and Medicaid Services lack reasonableness regarding likely success for fistula maturation in a heterogeneous, new-onset dialysis population. Here the various positions are examined from multiple perspectives.

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### **Nephrology**

Lattupalli, R., J. Yee and A. Kolluru (2008). "Nephrotoxicity of mala fide melamine: modern era milk scandal." ScientificWorldJournal **8**: 949-50. [Article Request Form](#)

Division of Nephrology, Henry Ford Hospital, Detroit, MI, USA. [RLATTUP1@hfhs.org](mailto:RLATTUP1@hfhs.org)

Nephrotoxicity of melamine was first suggested in pets leading to pet food recall in 2007. Melamine was deemed a very low human risk, until recent reports of acute renal failure from melamine adulterated milk in China. Melamine allows for fraudulent dilution of milk by inflating protein levels due to its high nitrogen content. Exact pathophysiology linking

melamine to kidney disease is unclear. It is advisable to avoid melamine until we gain a more scientific understanding of this new entity in humans.

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### **Nephrology**

Novak, J. E. and L. A. Szczech (2008). "Triumph and tragedy: anemia management in chronic kidney disease." Curr Opin Nephrol Hypertens **17**(6): 580-8. [PDF Full-Text](#)

Division of Nephrology and Hypertension, Department of Internal Medicine, Henry Ford Health System, Detroit, Michigan, USA; Division of Nephrology, Department of Medicine, Duke University Medical Center, Durham, North Carolina, USA.

**PURPOSE OF REVIEW:** Recent trial data have resulted in a reevaluation of the management of anemia in chronic kidney disease, including the use of erythropoiesis-stimulating agents, intravenous iron, and novel pharmaceuticals. In this review, we evaluate the latest research on anemia management in chronic kidney disease. **RECENT FINDINGS:** Clinical trials of erythropoiesis-stimulating agents indicate that targeting the complete correction of anemia in patients with chronic kidney disease results in a greater risk of morbidity and mortality despite improved hemoglobin and quality of life. Conversely, intravenous iron has been found effective and relatively well tolerated in treating anemia in chronic kidney disease, even in patients with elevated ferritin. New agents to manage anemia, including long-acting erythropoietin derivatives, are also in active development. **SUMMARY:** Erythropoiesis-stimulating agents should be used to target hemoglobin 11-12 g/dl in patients with chronic kidney disease. Intravenous iron may be beneficial for patients with hemoglobin less than 11 g/dl and transferrin saturation less than 25% despite elevated ferritin (500-1200 ng/ml). An upcoming placebo-controlled trial of darbepoetin should help to define the role of erythropoiesis-stimulating agents in chronic kidney disease.

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### **Nephrology**

Parasuraman, R. and K. K. Venkat (2008). "Utility of Estimated Glomerular Filtration Rate in Live Kidney Donation." Clin J Am Soc Nephrol. EPub Ahead of Print. [Article Request Form](#)

Division of Nephrology and Hypertension, Henry Ford Hospital, Detroit, Michigan.

Live kidney donation is considered safe; nevertheless, data supporting such claims are almost exclusively of white origin with very limited long-term outcomes in ethnic minority donors. This prospective observational study consisted of a total of 103 previous kidney donors (54 black and 49 white) with mean follow-up days of 743.5 +/- 603.9 for white and 845.1 +/- 668.5 for black donors. The black donors had a statistically significant greater loss of estimated GFR (eGFR; 39.8 ml/min per 1.73 m<sup>2</sup>) in comparison with white donors (30.4 ml/min per 1.73 m<sup>2</sup>; P = 0.001). In multivariate analysis, predonation eGFR of <100 ml/min and age at the time of donation were the significant predictors for postdonation eGFR <60 ml/min among black donors. Because eGFR using the Modification of Diet in Renal Disease 4 formula is not validated in live kidney donors, the significance of eGFR <60 ml/min per 1.73 m<sup>2</sup> in previous kidney donors is unclear. Long-term prospective study with a gold standard method such as iothalamate GFR measurement is needed to define the actual decrease in eGFR after kidney donation.

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### **Nephrology**

Russmann, S., L. Lamerato, S. P. Motsko, J. C. Pezzullo, M. D. Faber and J. K. Jones (2008). "Risk of Further Decline in Renal Function After the Use of Oral Sodium Phosphate or Polyethylene Glycol in Patients With a Preexisting Glomerular Filtration Rate Below 60 ml/min." Am J Gastroenterol. Epub Ahead of Print. [Article Request Form](#)

The Degge Group, Arlington, Virginia.

**OBJECTIVES:** The aim of this study was to estimate the risk of further creatinine increase in patients with preexisting renal disease after the use of oral sodium phosphate (OSP) versus polyethylene glycol (PEG), and to study usage patterns of OSP in relation to renal function. **METHODS:** A cohort study was done using clinical records and electronic patient information from the Henry Ford Health System (HFHS) in patients who had used either OSP or PEG for colonoscopy between February 1999 and April 2006. Among patients with an estimated GFR <60 ml/min before colonoscopy, we identified cases with an unexplained creatinine increase of  $\geq 0.5$  mg/dl within 14 days after colonoscopy. **RESULTS:** We identified 7,971 OSP and 1,511 PEG users. Relative use of OSP versus PEG decreased from 88.0% before 2004 to 48.4% in 2006. 70.2% of OSP users had no recorded creatinine determination within 60 days before colonoscopy, and this proportion did not decrease over time. The study population included 317 patients with a baseline GFR <60 ml/min, and we identified one case with an unexplained creatinine increase  $\geq 0.5$  mg/dl among 191 PEG users (0.5%) versus eight cases among 126 OSP users (6.3%). Unadjusted and adjusted relative risk estimates on comparing OSP with PEG were 12.1 (95% CI, 1.5-95.8) and 12.6 (95% CI, 1.5-106.5), respectively. **CONCLUSIONS:** In patients with preexisting renal disease, OSP use was associated with an increased risk of aggravated renal dysfunction versus PEG. Creatinine measurement with GFR estimation should be done before OSP administration in order to avoid its use in patients with renal disease.

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## **Neurology**

Demchuk, A. M., F. Khan, M. D. Hill, P. A. Barber, B. Silver, S. Patel and S. R. Levine (2008). "Importance of leukoaraiosis on CT for tissue plasminogen activator decision making: Evaluation of the NINDS rt-PA Stroke Study." Cerebrovascular Diseases **26**(2): 120-5. [Article Request Form](#)

**Background:** Leukoaraiosis is associated with microhemorrhages on T<sup>2</sup>\*-weighted magnetic resonance imaging of the brain. Such hemorrhages have been postulated to be responsible for symptomatic intracerebral hemorrhage (ICH) after thrombolytic treatment. We examined the relationship between small-vessel ischemic disease and symptomatic ICH within the NINDS rt-PA Stroke Study. **Methods:** Baseline CT scans from the NINDS rt-PA Stroke Study were re-evaluated retrospectively by blinded expert CT readers using the van Swieten Score (vSS) for leukoaraiosis. The scale examined the severity of white-matter changes on 3 serial CT slices and graded separately for the 2 distinct regions anterior and posterior to the central sulcus: 0 = no lesion, 1 = partly involving the white matter, and 2 = extending up to the cortex. **Results:** 603 CT scans were interpreted. The risk of symptomatic ICH increased with higher vSS in both the placebo and treatment groups. The absolute risk of symptomatic hemorrhage was 7.9% in the rt-PA-treated cohort among patients with severe white-matter disease (vSS = 3-4) versus 2.9% receiving placebo. Among severe leukoaraiosis patients (vSS = 3-4), no differential treatment effect was seen with rt-PA patients achieving better outcomes than placebo, modified Rankin score 0-1 in 31.6% of rt-PA-treated versus 14.7% of placebo-treated patients. **Conclusion:** The results from the present study do not support the concept that leukoaraiosis present on baseline noncontrast CT scanning is critical to thrombolysis decision making in the first 3 h from symptom onset. No clear leukoaraiosis threshold was identified below which no benefit or harm could be seen from intravenous rt-PA therapy.

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## Neurology

Hacein-Bey, L. and P. N. Varelas (2008). "Angioplasty and stenting for cerebrovascular disease: Current status." Neurosurg Clin N Am **19**(3): 433. [Article Request Form](#)

Radiol Associates Sacramento Med Grp Inc., Sacramento, CA 95816

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## Neurology

Liu, X. S., M. Chopp, X. G. Zhang, R. L. Zhang, B. Buller, A. Hozeska-Solgot, S. R. Gregg and Z. G. Zhang (2008). "Gene profiles and electrophysiology of doublecortin-expressing cells in the subventricular zone after ischemic stroke." J Cereb Blood Flow Metab. Epub Ahead of Print. [Article Request Form](#)

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

Stroke increases neuroblasts in the subventricular zone (SVZ) of the lateral ventricle and these neuroblasts migrate toward the ischemic boundary to replace damaged neurons. Using brain slices from the nonischemic adult rat and transgenic mice that expressed enhanced green fluorescent protein (EGFP) concomitantly with doublecortin (DCX), a marker for migrating neuroblasts, we recorded electrophysiological characteristics while simultaneously analyzing the gene expression in single SVZ cells. We found that SVZ cells expressing the DCX gene from the nonischemic rat had a mean resting membrane potential (RMP) of -30 mV. DCX-EGFP-positive cells in the nonischemic SVZ of the transgenic mouse had a mean RMP of -25+/-7 mV and did not exhibit Na(+) currents, characteristic of immature neurons. However, DCX-EGFP-positive cells in the ischemic SVZ exhibited a hyperpolarized mean RMP of -54+/-18 mV and displayed Na(+) currents, indicative of more mature neurons. Single-cell multiplex RT-PCR analysis revealed that DCX-EGFP-positive cells in the nonischemic SVZ of the transgenic mouse expressed high neural progenitor marker genes, Sox2 and nestin, but not mature neuronal marker genes. In contrast, DCX-EGFP-positive cells in the ischemic SVZ expressed tyrosine hydroxylase, a mature neuronal marker gene. Together, these data indicate that stroke changes gene profiles and the electrophysiology of migrating neuroblasts. Journal of Cerebral Blood Flow & Metabolism advance online publication, 15 October 2008; doi:10.1038/jcbfm.2008.119.

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## Neurology

Varelas, P. N. (2008). "How I treat status epilepticus in the Neuro-ICU." Neurocrit Care **9**(1): 153-7. [Article Request Form](#)

Department of Neurology, Henry Ford Hospital, K-11, 2799 West Grand Blvd, Detroit, MI 48202, USA. [Varelas@neuro.hfh.edu](mailto:Varelas@neuro.hfh.edu)

Status epilepticus still remains a formidable adversary to neurointensivists. Although the majority of cases admitted to the Neuro-ICU are easily controlled with one or two antiepileptic drug defense lines, several cases become refractory and end up receiving general anesthetics for days or weeks with significant morbidity. Treatment algorithms have been published and should be followed, but in many cases they are inadequate because, especially in the distal branches of the treatment tree, are based on anecdotal data or small series of patients. In addition, a double-blind, randomized-controlled study in status has not been done for many years and solid data are lacking for the newer antiepileptics. Therefore, in the moderately to severely refractory cases, status treatment is based on personal previous experience and becomes an art more than a science. In

this review of a difficult case, we discuss some fine details of the treatment provided and emphasize the multidisciplinary approach that should be followed including involvement of neurointensivists, epileptologists, electroencephalographers, and neurosurgeons.

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## Neurology

Zacharek, A., J. Chen, X. Cui, Y. Yang and M. Chopp (2008). "Simvastatin Increases Notch Signaling Activity and Promotes Arteriogenesis After Stroke." Stroke. [Article Request Form](#)

From Department of Neurology, Henry Ford Hospital, Detroit, Mich;  
Department of Physics, Oakland University, Rochester, Mich.

**BACKGROUND AND PURPOSE:** Notch signaling activity regulates arteriogenesis. Presenilin 1 (PS1) mediates Notch signaling activity via cleavage of Notch, liberating Notch intracellular domain (NICD). We tested the hypothesis that simvastatin enhances arteriogenesis after stroke by increasing PS1 activation of the Notch signaling pathway. **METHODS:** Rats were subjected to middle cerebral artery occlusion (MCAo) and treated with or without simvastatin (1 mg/kg) starting 24 hours after stroke and daily for 7 days; they were euthanized 14 days after stroke. Immunostaining, Western blot, and real-time polymerase chain reaction assays were performed. **RESULTS:** Simvastatin significantly increased arterial diameter, density, and vascular smooth muscle cell proliferation, and upregulated PS1, Notch1, and NICD expression in the ischemic border tissue and in the cerebral arteries compared with MCAo control rats, respectively. However, simvastatin did not increase arteriogenesis, PS1, and NICD expression in sham control animals. To investigate the mechanisms of simvastatin-induced arteriogenesis, primary cerebral artery cultures were used. Rats were subjected to MCAo and treated with or without simvastatin daily for 7 days. The cerebral arteries derived from these stroke rats were cultured in matrigel and treated with or without a gamma40-secretase inhibitor II, which blocks Notch signaling activity, inhibiting NICD production. Arterial cell migration was measured. simvastatin treatment significantly increased arterial cell migration compared to control MCAo artery, whereas inhibition of Notch signaling activity by the gamma40-secretase inhibitor II significantly attenuated simvastatin-induced arterial cell migration. **CONCLUSIONS:** These data indicate that simvastatin increases arteriogenesis after stroke, and that simvastatin upregulation of PS1 expression and Notch signaling activity may facilitate an increase in arteriogenesis.

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## Neurology

Zhang, R. L., C. Zhang, L. Zhang, C. Roberts, M. Lu, A. Kapke, Y. Cui, M. Ninomiya, T. Nagafuji, B. Alcala, Z. G. Zhang and M. Chopp (2008). "Synergistic effect of an endothelin type A receptor antagonist, S-0139, with rtPA on the neuroprotection after embolic stroke." Stroke **39**(10): 2830-6. [PDF Full-Text](#)

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

**BACKGROUND AND PURPOSE:** Using a model of embolic stroke, the present study tested the hypothesis that blockage of endothelin-1 with S-0139, a specific endothelin type A receptor (ET(A)) antagonist, enhances the neuroprotective effect of recombinant tissue plasminogen activator (rtPA) by suppressing molecules that mediate thrombosis and blood brain barrier (BBB) disruption induced by ischemia and rtPA. **METHODS:** Rats (n=104) subjected to embolic middle cerebral artery (MCA) occlusion were randomly divided into 1 of 4 infusion groups with 26 rats per group: (1) the control group in which rats were administered saline, (2) the monotherapy rtPA group in which rtPA was intravenously administered at a dose of 10 mg/kg 4 hours after MCA occlusion, (3) the monotherapy S-0139 group in which S-0139 was intravenously given 2 hours after MCA

occlusion, and (4) the combination of rtPA +S-0139 group in which S-0139 and rtPA were given 2 and 4 hours after MCA occlusion, respectively. Measurements of infarct volume and parenchymal hemorrhage, behavioral outcome, and immunostaining were performed on rats euthanized 1 and 7 days after stroke. RESULTS: The combination therapy of S-0139 and rtPA significantly ( $P<0.01$ ) reduced infarct volume (24.8 $\pm$ 0.9% versus 33.8 $\pm$ 1.5% in control) and hemorrhagic area (7.1 $\pm$ 6.1 microm<sup>2</sup>) versus 36.5 $\pm$ 19.2 microm<sup>2</sup>) and improved functional recovery compared with control saline-treated animals. Immunostaining analysis revealed that the combination therapy had synergistically suppressed ischemia- and rtPA-induced ICAM-1, protease-activated receptor 1 (PAR-1), as well as accumulation of platelets in cerebral microvessels. Furthermore, the combination treatment synergistically reduced loss of laminin, ZO1, and occludin in cerebral vessels. CONCLUSIONS: These data suggest that S-0139 provides the neuroprotection by suppressing ischemia- and rtPA-triggered molecules that evoke thrombosis and BBB disruption.

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### **Neurology**

Zhang, R. L., Z. G. Zhang and M. Chopp (2008). "Ischemic stroke and neurogenesis in the subventricular zone." Neuropharmacology **55**(3): 345-52. [Article Request Form](#)

Department of Neurology, Henry Ford Health Sciences Center, Detroit, MI 48202, USA.

The subventricular zone (SVZ) of the lateral ventricle contains neural stem and progenitor cells that generate neuroblasts, which migrate to the olfactory bulb where they differentiate into interneurons. Ischemic stroke induces neurogenesis in the SVZ and these cells migrate to the boundary of the ischemic lesion. This article reviews current data on cyto kinetics, signaling pathways and vascular niche that are involved in processes of proliferation, differentiation, and migration of neural progenitor cells after stroke.

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### **Neurosurgery**

McIntosh, K. and N. Roosen (2008). "Gunshot wounds of the brain and skull, part 1: A neurosurgical perspective." Br J Neurosci Nurs **4**(6): 286-91. [Article Request Form](#)

Henry Ford Health System, Department of Neurosurgery, Detroit, MI

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### **Neurosurgery**

Wu, H., D. Lu, H. Jiang, Y. Xiong, C. Qu, B. Li, A. Mahmood, D. Zhou and M. Chopp (2008). "Increase in phosphorylation of Akt and its downstream signaling targets and suppression of apoptosis by simvastatin after traumatic brain injury." J Neurosurg **109**(4): 691-8. [Article Request Form](#)

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

OBJECT: In their previous studies, the authors found that simvastatin treatment of traumatic brain injury (TBI) in rats had beneficial effects on spatial learning functions. In the current study they wanted to determine whether simvastatin suppressed neuronal cell apoptosis after TBI, and if so, they wanted to examine the underlying mechanisms of this process. METHODS: Saline or simvastatin (1 mg/kg) was administered orally to rats

starting on Day 1 after TBI and then daily for 14 days. Modified Neurological Severity Scores were used to evaluate the sensory motor functional recovery. Rats were killed at 1, 3, 7, 14, and 35 days after treatment, and brain tissue was harvested for terminal deoxynucleotidyl nick-end labeling (TUNEL) staining, caspase-3 activity assay, and Western blot analysis. RESULTS: Simvastatin significantly decreased the modified Neurological Severity Scores from Days 7 to 35 after TBI, significantly reduced the number of TUNEL-positive cells at Day 3, suppressed the caspase-3 activity at Days 1 and 3 after TBI, and increased phosphorylation of Akt as well as Forkhead transcription factor 1, inhibitory-kappaB, and endothelial nitric oxide synthase, which are the downstream targets of the prosurvival Akt signaling protein. CONCLUSIONS: These data suggested that simvastatin reduces the apoptosis in neuronal cells and improves the sensory motor function recovery after TBI. These beneficial effects of simvastatin may be mediated through activation of Akt, Forkhead transcription factor 1 and nuclear factor-kappaB signaling pathways, which suppress the activation of caspase-3 and apoptotic cell death, and thereby, lead to neuronal function recovery after TBI.

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### **Neurosurgery**

Xiong, Y., D. Lu, C. Qu, A. Goussev, T. Schallert, A. Mahmood and M. Chopp (2008). "Effects of erythropoietin on reducing brain damage and improving functional outcome after traumatic brain injury in mice." *J Neurosurg* **109**(3): 510-21. [PDF Full-Text](#)

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

OBJECT: This study was designed to investigate the beneficial effects of recombinant human erythropoietin (rhEPO) treatment of traumatic brain injury (TBI) in mice. METHODS: Adult male C57BL/6 mice were divided into 3 groups: 1) the saline group (TBI and saline [13 mice]); 2) EPO group (TBI and rhEPO [12]); and 3) sham group (sham and rhEPO [8]). Traumatic brain injury was induced by controlled cortical impact. Bromodeoxyuridine (100 mg/kg) was injected daily for 10 days, starting 1 day after injury, for labeling proliferating cells. Recombinant human erythropoietin was administered intraperitoneally at 6 hours and at 3 and 7 days post-TBI (5000 U/kg body weight, total dosage 15,000 U/kg). Neurological function was assessed using the Morris water maze and footfault tests. Animals were killed 35 days after injury, and brain sections were stained for immunohistochemical evaluation. RESULTS: Traumatic brain injury caused tissue loss in the cortex and cell loss in the dentate gyrus (DG) as well as impairment of sensorimotor function (footfault testing) and spatial learning (Morris water maze). Traumatic brain injury alone stimulated cell proliferation and angiogenesis. Compared with saline treatment, rhEPO significantly reduced lesion volume in the cortex and cell loss in the DG after TBI and substantially improved recovery of sensorimotor function and spatial learning performance. It enhanced neurogenesis in the injured cortex and the DG. CONCLUSIONS: Recombinant human erythropoietin initiated 6 hours post-TBI provided neuroprotection by decreasing lesion volume and cell loss as well as neurorestoration by enhancing neurogenesis, subsequently improving sensorimotor and spatial learning function. It is a promising neuroprotective and neurorestorative agent for TBI and warrants further investigation.

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### **Neurosurgery**

Zuniga, R. M., R. Torcuator, R. Jain, J. Anderson, T. Doyle, S. Ellika, L. Schultz and T. Mikkelsen (2008). "Efficacy, safety and patterns of response and recurrence in patients with recurrent high-grade gliomas treated with bevacizumab plus irinotecan." *J Neurooncol*. Epub Ahead of Print. *Sladen has electronic subscription. Issue for this article not available online at the time of this publication.*

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### Otolaryngology

Cheng, J., S. Qiu, U. Raju, S. R. Wolman and M. J. Worsham (2008). "Benign breast disease heterogeneity: association with histopathology, age, and ethnicity." Breast Cancer Res Treat **111**(2): 289-96. [PDF Full-Text](#)

Department of Otolaryngology, Head and Neck Surgery, Henry Ford Hospital, Detroit, MI, USA.

**BACKGROUND:** Benign breast biopsies with concurrent multiple benign lesions with different histopathologic diagnoses were termed heterogeneous benign breast disease (HBBD). Multiplicity of benign breast disease (BBD) lesions in a biopsy is a risk factor for progression to breast cancer (BC). Elucidation of the biological characteristics and clinical implications of HBBD may also be relevant to the refinement of risks for BC in women with a BBD diagnosis. **DESIGN:** In this study, we investigated the association of HBBD with histopathology, age, and ethnicity. A cohort of 4,341 women, 1,208 African Americans and 3,133 Caucasians, diagnosed with BBD, was identified after examination of an excisional breast biopsy. BBD biopsies were categorized as nonproliferative (NP, low risk or risk 1 lesions), proliferative without atypia (P, intermediate risk or risk 2 lesions), and proliferative with atypia (AH, high risk or risk 3 lesions). A BBD biopsy with only a single BBD lesion was termed simple BBD (SBBD). BBD biopsies with multiple lesions were further classified as single level HBBD (SL-HBBD) if the concurrent lesions were within the same risk level, or as multiple level HBBD (ML-HBBD) if lesions fell into more than one risk group. **RESULTS:** In this cohort, 69% of women with a BBD diagnosis fit the HBBD criteria. Among women with HBBD, ML-HBBD was almost three times more prevalent than SL-HBBD and was significantly more likely to be composed of risk 2 and risk 3 lesions. The likelihood of HBBD was 57% higher in Caucasian American women than in African American women with BBD (OR 1.57; 95% CI: 1.37, 1.81). The average lesion number in HBBD was directly proportional to increasing lesion risk ( $P < 0.001$ ). Compared to women with risk 1 lesions, the likelihood of HBBD was 5.59 (95% CI: 4.85-6.44) and 17.0 (95% CI: 10.2-28.5) times higher when risk 2 and risk 3 lesions, respectively, were present. Women in the age range of 46-55 years and >55 years had a 3.12 (95% CI: 2.59, 3.75) and a 2.28 (95% CI: 1.94, 2.68) fold higher likelihood of HBBD compared to those  $< \text{or} = 45$  years. Significant interaction was found between concurrent lesion levels and age ( $P < 0.01$ ). The likelihood of HBBD was considerably higher across all age groups for risk 3 lesions. Compared to the reference (risk 1, age  $< \text{or} = 45$ ), the likelihood of HBBD for risk 2 lesions was 4.4 times greater (95% CI: 3.70, 5.33) in women  $< \text{or} = 45$  YEARS, BUT THAT LIKELIHOOD INCREASED TO 17.6 (95% CI: 12.8, 24.2) AND 13.4 (95% CI: 10.1, 17.9) TIMES IN WOMEN OF 46-55 AND >55 YEARS, RESPECTIVELY. **CONCLUSION:** HBBD is more prevalent in Caucasian American women than in African American women. Women with higher risk BBD lesions are more likely to have HBBD. Lesion number and higher risk BBD lesions are significantly correlated with ML-HBBD. Additionally, the associations of HBBD and lesion risk level are modified by age.

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### Otolaryngology

Seidman, M. D. (2008). "Response to: Letter to the Editor, References in history of tympanoplasty from Albert Mudry." Otolaryngol Head Neck Surg **139**(4): 611. [Article Request Form](#)

Henry Ford Health System, Otolaryngology-HNS, West Bloomfield, MI.

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### **Otolaryngology**

Worsham, M. J., U. Raju, M. Lu, A. Kapke, A. Botttrel, J. Cheng, V. Shah, A. Savera and S. R. Wolman (2008). "Risk factors for breast cancer from benign breast disease in a diverse population." Breast Cancer Res Treat. EPub Ahead of Print. [Article Request Form](#)

Department of Otolaryngology/Head and Neck Surgery, Henry Ford Health System, 1 Ford Place, 1D, Detroit, MI, 48202, USA, [mworsha1@hfhs.org](mailto:mworsha1@hfhs.org).

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

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### **Pathology**

Cancer Genome Atlas Research Network (2008). "Comprehensive genomic characterization defines human glioblastoma genes and core pathways." Nature **455**(7216): 1061-8. [PDF Full-Text](#)

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### **Plastic Surgery**

Harrington, C. B., A. Siddiqui and M. Feuerstein (2008). "Workstyle predicts pain and work outcomes in surgical and non surgical management of hand pain." Annals of Behavioral Medicine **35**: S123-S123. [PDF Full-Text](#)

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

Ernst, A., M. Simoff, D. Ost, Y. Goldman and F. J. F. Herth (2008). "Prospective risk-adjusted morbidity and mortality outcome analysis after therapeutic bronchoscopic procedures - Results of a multi-institutional outcomes database." Chest **134**(3): 514-519. [PDF Full-Text](#)

Introduction: Interest in databases is growing to allow for outcomes research, assess health-care quality, and determine best practices and resource allocation, and they, are increasingly considered as a tool to potentially tie reimbursement to outcome parameters. Little is known about resource use and risk-adjusted morbidity and mortality after therapeutic bronchoscopic interventions. Methods: Data were extracted and reviewed from an ongoing prospective, multi-institutional outcomes database for therapeutic bronchoscopic interventions. All consecutive patients are entered into this database, and information on demographics, indications, procedures and anesthesia, comorbidities and general health status, urgency of intervention, morbidity and mortality to 30 days, increase in levels of care, and procedural resources is documented. Results: From December 2005 to May 2007, 554 therapeutic procedures were performed in four hospitals. Most procedures were done under general anesthesia (n = 362) and rigid bronchoscopy (n = 483), and the most common intervention was airway stent placement (n = 258). Forty-two percent of procedures were done urgently or emergently. Complications were common (19.8%), and 30-day mortality was 7.8%, correlating with underlying health status and urgency of intervention. Discussion: Prospective and ongoing data analysis for bronchoscopic procedures is feasible and valuable. Risk-adjusted and disease-specific outcomes can be documented and potentially used for quality assessment, benchmarking, and quality improvement initiatives. Appropriate use of resources and effect of interventions can be documented. Extending the number of participating centers as well as inclusion of quality of life tools and technical success are the next steps.

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

Khalid, I., E. Zoratti, L. Stagner, A. D. Betensley, H. Nemeh and L. Allenspach (2008). "Transfer of peanut allergy from the donor to a lung transplant recipient." J Heart Lung Transplant **27**(10): 1162-4. [Article Request Form](#)

Department of Pulmonary and Critical Care Medicine, Henry Ford Health System, Detroit, Michigan 48202, USA. [doc\\_ik@yahoo.com](mailto:doc_ik@yahoo.com)

Among solid organs, transfer of peanut allergy from donor to recipient has been implicated after liver transplantation. We report the first case in which such transfer occurred after a lung transplant. A 42-year-old woman with history of sarcoidosis underwent a successful bilateral lung transplant from a donor who died from anaphylactic shock after eating peanut-related food. Seven months later, she ate a peanut butter cookie at a transplant support group meeting. Immediately thereafter, she developed an anaphylactic reaction, but survived with prompt treatment. During subsequent follow-up, she could recall three prior episodes of wheezing and difficulty breathing after eating peanut-related foods. The first episode occurred 4 days after the transplant. Prior to her transplant, she never had problems eating peanuts. Skin-prick testing confirmed peanut sensitization. She avoided peanuts and, although her skin-prick test became negative, she still manifested peanut allergy when formally challenged orally with the food. She was advised to continue abstaining from all peanut-related foods. This case emphasizes the importance of considering donor allergy transfer when caring for all solid-organ transplant recipients in order to avoid a life-threatening event.

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### **Rheumatology**

Somers, E. C., E. E. Lewis, E. M. Bodkin, D. Shaltis, W. Marder, P. C. Cagnoli, Y. J. Wong, P. DeGuire, C. Gordon, C. G. Helmick, J. Leisen, J. P. Dhar and W. J. McCune (2008). "Michigan lupus epidemiology & surveillance (MILES) program: Neurologic involvement among SLE patients in a population-based registry." Arthritis Rheumatism **58**(9): S637-S638. [Article Request Form](#)

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### **Rheumatology**

Somers, E. C., E. E. Lewis, D. Shaltis, E. M. Bodkin, P. C. Cagnoli, W. Marder, Y. J. Wong, P. DeGuire, C. Gordon, C. G. Helmick, J. Leisen, J. P. Dhar and W. J. McCune (2008). "Michigan lupus epidemiology & surveillance (MILES) program: Features of SLE in a population-based registry of pediatric-onset patients." Arthritis Rheumatism **58**(9): S253-S254. [Article Request Form](#)

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### **Sleep Medicine**

Burger, A., R. Stout, M. Gillis, T. Roehrs, M. Lumley and T. Roth (2008). "Unique rem rebound and daytime hyperarousal following sleep restriction in fibromyalgia patients." Annals of Behavioral Medicine **35**: S111-S111. [PDF Full-Text](#)

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### **Sleep Medicine**

Drake, C. L., J. R. L. Schwartz and T. Roth (2008). "The evolution of insomnia in relation to comorbidity." Psychiatric Annals **38**(9): 621-626. [Article Request Form](#)

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### **Sleep Medicine**

Phillips, B. A., N. A. Collop, C. Drake, F. Consens, A. N. Vgontzas and T. E. Weaver (2008). "Sleep disorders and medical conditions in women." J Women's Health **17**(7): 1191-9. [Article Request Form](#)

Sleep disorders affect women differently than they affect men and may have different manifestations and prevalences. With regard to obstructive sleep apnea (OSA), variations in symptoms may cause misdiagnoses and delay of appropriate treatment. The prevalence of OSA appears to increase markedly after the time of menopause. Although OSA as defined by the numbers of apneas/hypopneas may be less severe in women, its consequences are similar and perhaps worse. Therapeutic issues related to gender should be factored into the management of OSA. The prevalence of insomnia is significantly greater in women than in men throughout most of the life span. The ratio of insomnia in women to men is approximately 1.4:1.0, but the difference is minimal before puberty and increases steadily with age. Although much of the higher prevalence of insomnia in women may be attributable to the hormonal or psychological changes associated with major life transitions, some of the gender differences may result from the higher prevalence of depression and pain in women. Insomnia's negative impact on quality of life is important to address in women, given the high relative prevalence of insomnia as well as the comorbid disorders in this population. Gender differences in etiology and symptom manifestation in narcolepsy remain understudied in humans. There is little available scientific information to evaluate the clinical significance and specific consequences of the diagnosis of narcolepsy in women. Restless legs syndrome (RLS) is characterized by an urge to move the legs or other limbs during periods of rest or inactivity and may affect as much as 10% of the population. This condition is more likely

to afflict women than men, and its risk is increased by pregnancy. Although RLS is associated with impaired quality of life, highly effective treatment is available.

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### **Sleep Medicine**

Richardson, G. S., P. C. Zee, S. Wang-Weigand, L. Rodriguez and X. Peng (2008). "Circadian phase-shifting effects of repeated ramelteon administration in healthy adults." J Clin Sleep Med 4(5): 456-61. [PDF Full-Text](#)

Henry Ford Hospital, Sleep Center, 2799 West Grand Blvd., CFP-3, Detroit, MI 48202, USA. [grichar1@gmail.com](mailto:grichar1@gmail.com)

STUDY OBJECTIVES: To assess the ability of repeated daily oral ramelteon to facilitate re-entrainment of human circadian rhythms after an imposed phase advance of the sleep-wake cycle. METHODS: A total of 75 healthy adult volunteers aged 18-45 years remained in a sleep laboratory for 6 days and 5 nights; a 5-h phase advance in their sleep-wake cycle was imposed under dim-light conditions. Oral ramelteon (1,2, 4, or 8 mg once daily for 4 days) or placebo was administered 30 min before bedtime. The primary endpoint was the phase of the circadian rhythm as assessed by the time at which salivary melatonin concentrations declined below 3 pg/mL after morning awakening (dim-light melatonin offset [DLMoff]). RESULTS: After 4 days of once-daily treatment, participants receiving 1, 2, or 4 mg ramelteon exhibited statistically significant phase shifts in DLMoff of -88.0 (16.6), -80.5 (14.8), and -90.5 (15.2) minutes respectively, versus -7.1 (18.6) minutes for placebo (least-squares mean(SEM),  $p = 0.002$ ,  $p = 0.003$ ,  $p = 0.001$ , respectively). Change in DLMoff for the 8 mg dose of ramelteon, -27.9 (16.4) minutes, was not significantly different than that for placebo ( $p = 0.392$ ). CONCLUSIONS: Ramelteon (1, 2, or 4 mg per day) administered before bedtime significantly advanced the phase of the circadian rhythm after a 5-h phase advance in the sleep-wake cycle. These findings suggest that ramelteon has potential as a specific therapy for circadian rhythm sleep disorders.

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### **Sleep Medicine**

Roth, T. (2008). "Insomnia and sleep-related disorders." Psychiatric Annals 38(9): 575-+. [Article Request Form](#)

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### **Surgery**

Berry, S. D., C. J. Thomas, J. H. Patton, A. J. Falvo, J. Ritz, J. Jordan and I. S. Rubinfeld (2008). "Acute care surgeons: Not just a title - improved survival in elderly patients requiring operative intervention." J Am Coll Surg 207(3): S48-S48. [PDF Full-Text](#)

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### **Surgery**

Carlin, A. M., E. A. O'Connor, J. A. Genaw and S. Kavar (2008). "Preoperative weight loss is not a predictor of postoperative weight loss after laparoscopic Roux-en-Y gastric bypass." Surg Obes Relat Dis 4(4): 481-5. [Article Request Form](#)

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

**BACKGROUND:** Identification of preoperative predictors of weight loss after laparoscopic Roux-en-Y gastric bypass (LRYGB) can lead to improved clinical outcomes. The purpose of this study was to determine whether preoperative weight loss was associated with improved percentage of excess weight loss (%EWL) 1 year after LRYGB. **METHODS:** A retrospective analysis was performed on the data from 295 patients who had undergone LRYGB at our institution from July 2004 to November 2005. Routine preoperative weight loss goals were implemented to facilitate the laparoscopic approach and ensure compliance with an appropriate nutritional and exercise program. Patients with an initial consultation BMI of <50, 50-59, and > or =60 kg/m<sup>2</sup> were given weight loss goals of 5 lb and 5% and 10% of body weight, respectively. **RESULTS:** The mean age was 45 +/- 10 years, and 89% were women and 70% were white. The mean BMI at the initial consultation was 51 +/- 7 kg/m<sup>2</sup>. A significant inverse correlation was found between the preoperative BMI and %EWL at 1 year postoperative (P <.001). When controlling for BMI, no correlation was found between the %EWL and percentage of preoperative weight loss or attainment of the weight loss goals. The weight loss goals were met or surpassed by 79% of patients, and the mean %EWL at 1 year was 66%. Whites had greater %EWL at 1 year postoperatively compared with African Americans (67% versus 61%; P = .002). When controlling for age, gender, race, and consultation BMI, the preoperative weight loss did not predict for the %EWL at 1 year. **CONCLUSION:** The results of this study have shown that preoperative weight loss does not predict postoperative weight loss 1 year after LRYGB. A lower BMI, younger age, and white race predicted better %EWL.

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### **Surgery**

Kakkos, S. K., J. A. Caprini, G. Geroulakos, A. N. Nicolaidis, G. P. Stansby and D. J. Reddy (2008). "Combined intermittent pneumatic leg compression and pharmacological prophylaxis for prevention of venous thromboembolism in high-risk patients." Cochrane Database Syst Rev(4): CD005258. [PDF Full-Text](#)

Division of Vascular Surgery, Department of Surgery, Henry Ford Hospital, 2799 W. Grand Boulevard, Detroit, Michigan, USA, 28202.

**BACKGROUND:** It has been suggested that combined modalities (methods of treatment) are more effective than single modalities in preventing venous thromboembolism (defined as deep vein thrombosis and pulmonary embolism, or both) in high-risk patients. **OBJECTIVES:** To assess the efficacy of intermittent pneumatic leg compression combined with pharmacological prophylaxis versus single modalities in preventing venous thromboembolism in high-risk patients. **SEARCH STRATEGY:** The Cochrane Peripheral Vascular Diseases (PVD) Group searched their Specialized Register (last searched 17 July 2007) and the Cochrane Central Register of Controlled Trials (CENTRAL) (last searched The Cochrane Library 2008, Issue 3). We searched the reference lists of relevant articles to identify additional trials. **SELECTION CRITERIA:** Randomized controlled trials (RCTs) or controlled clinical trials (CCTs) of combined intermittent pneumatic leg compression and pharmacological interventions used to prevent venous thromboembolism in high-risk patients. **DATA COLLECTION AND ANALYSIS:** Data extraction was undertaken independently by two review authors using data extraction sheets. **MAIN RESULTS:** Eleven studies, six of them randomized controlled trials, were identified. The trials included 7431 patients, in total. Compared with compression alone, the use of combined modalities reduced significantly the incidence of both symptomatic pulmonary embolism (PE) (from about 3% to 1%; odds ratio (OR) 0.39, 95% confidence interval (CI) 0.25 to 0.63) and deep vein thrombosis (DVT) (from about 4% to 1%; OR 0.43, 95% CI 0.24 to 0.76). Compared with pharmacological prophylaxis alone, the use of combined modalities significantly reduced the incidence of DVT (from 4.21% to 0.65%; OR 0.16, 95% CI 0.07 to 0.34) but the included studies were underpowered with regard to PE. The comparison of compression plus pharmacological prophylaxis versus compression plus aspirin showed a non-significant reduction in PE and DVT in favor of the former group. Repeat analysis restricted to the RCTs confirmed the above findings. **AUTHORS' CONCLUSIONS:** Compared with compression alone,

combined prophylactic modalities decrease significantly the incidence of venous thromboembolism. Compared with pharmacological prophylaxis alone, combined modalities reduce significantly the incidence of DVT but the effect on PE is unknown. The results of the current review support, especially in high-risk patients, the use of combined modalities. More studies on their role in PE prevention, compared with pharmacological prophylaxis alone, are urgently needed.

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### **Surgery**

Kakkos, S. K. and A. D. Shepard (2008). "Regarding "Delayed presentation of aortic injury by pedicle screws: Report of two cases and review of the literature."" J Vasc Surg **48**(4): 1068. [PDF Full-Text](#)

Henry Ford Hospital, Detroit, MI 48202

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### **Surgery**

Miller, J. M. and V. Velanovich (2008). "The natural language of the physician's clinical note in outcomes assessment: A qualitative analysis of the medical record." J Am Coll Surg **207**(3): S73-S73. [PDF Full-Text](#)

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### **Surgery**

O'Connor, E. A. and A. M. Carlin (2008). "Lack of correlation between variation in small-volume gastric pouch size and weight loss after laparoscopic Roux-en-Y gastric bypass." Surg Obes Relat Dis **4**(3): 399-403. [Article Request Form](#)

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

**BACKGROUND:** Controversy exists in published reports regarding the influence of gastric pouch size on weight loss after gastric bypass (GB). The purpose of this study was to determine whether variations in the anatomic size of small-volume ( $\leq 20$  cm<sup>3</sup>) gastric pouches correlate with weight loss 1 year after laparoscopic GB. **METHODS:** We prospectively collected intraoperative data on gastric pouch size during laparoscopic GB in 231 morbidly obese patients. A divided, vertical, lesser curve-based gastric pouch was created using an orogastric tube for size and diameter determination. The height of the cylindrical pouch was measured by the number of staple fires. **RESULTS:** The mean age was 45 +/- 10 years, 90% were women, and 68% were white. The mean preoperative body mass index was 48 +/- 6 kg/m<sup>2</sup>. The percentage of excess weight loss (%EWL) 1 year after GB was 66%. The calculated gastric pouch volume was 10-20 cm<sup>3</sup>. No significant difference was found in the %EWL at 1 year when stratified by gastric pouch size. The pouch size was not dependent on age, gender, preoperative weight, or body mass index. A significant inverse correlation was found between the %EWL and both preoperative weight and body mass index ( $P < .001$ ). Blacks had significantly smaller gastric pouches than whites ( $P = .004$ ); however, whites had a significantly greater %EWL at 1 year compared with blacks (67% versus 61%;  $P = .016$ ). **CONCLUSION:** With construction of divided, vertical, lesser curve-based small-volume ( $< \text{ or } = 20$  cm<sup>3</sup>) gastric pouches, the actual size of the gastric pouch did not correlate with the %EWL at 1 year after laparoscopic GB.

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### **Surgery**

Rajda, C., D. Dereczyk and P. Kunkel (2008). "Propofol infusion syndrome." J Trauma Nurs **15**(3): 118-22. [PDF Full-Text](#)

Department of Trauma Services, Henry Ford Hospital, Detroit, Michigan 48202, USA. [crajda1@hfhs.org](mailto:crajda1@hfhs.org)

Propofol (Diprivan) is an intravenous sedative hypnotic that is used in the induction and maintenance of anesthesia and sedation. High-dose infusions have been associated with several serious adverse effects and, when combined, they are known as propofol infusion syndrome (PRIS). Although PRIS is rare, it is frequently fatal if not identified early. The purpose of this article is to raise practitioner awareness to this syndrome, with recommendations for early identification, prevention, and treatment of PRIS.

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### **Urology**

Eun, D., A. Bhandari, R. Boris, K. Lyall, M. Bhandari, M. Menon and C. G. Rogers (2008). "A novel technique for creating solid renal pseudotumors and renal vein-inferior vena caval pseudothrombus in a porcine and cadaveric model." J Urol **180**(4): 1510-4. [PDF Full-Text](#)

Vattikuti Urology Institute, Henry Ford Hospital, Detroit, Michigan 48202-2689, USA.

**PURPOSE:** We developed a simple means to replicate kidney tumors in an animal and cadaver model that could be used to create pseudotumors of different sizes and locations for use in surgical training. **MATERIALS AND METHODS:** Various substances were injected ex vivo into the parenchyma of porcine kidneys to identify an optimal pseudotumor model. Renal pseudotumors were created percutaneously and endoscopically using 8 live pigs and a human cadaver model. A renal vein pseudothrombus porcine model was also created by injecting pseudothrombus material into the renal vein after renal hilar clamping. Procedures performed on pseudotumors included robotic partial nephrectomy, percutaneous biopsy and robotic nephrectomy with renal vein thrombectomy. All specimens were analyzed after resection. **RESULTS:** The most ideal pseudotumor models were created from a mixture of gelatin, Metamucil and methylene blue (metagel) or from Kromopan hydrocolloid. We created 33 tumors 0.5 to 3.5 cm in size (mean 2.8). All tumors were a solid palpable mass on gross examination and ultrasonography revealed clearly visible hyperechoic lesions in 30 of 33. A renal vein tumor pseudothrombus model was successfully created in 3 pigs. We successfully performed robotic excision of pseudotumors, including partial nephrectomy for 16 and radical nephrectomy with renal vein thrombectomy for 3. Percutaneous needle core biopsy under ultrasound guidance was also successfully performed. **CONCLUSIONS:** We describe what is to our knowledge a novel technique of creating solid renal tumors and tumor thrombi that can be used for training in minimally invasive kidney surgery.

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### **Urology**

Kumar, V., S. Mohanty, A. Kumar, R. P. Misra, M. Santosham, S. Awasthi, A. H. Baqui, P. Singh, V. Singh, R. C. Ahuja, J. V. Singh, G. K. Malik, S. Ahmed, R. E. Black, M. Bhandari and G. L. Darmstadt (2008). "Effect of community-based behaviour change management on neonatal mortality in Shivgarh, Uttar Pradesh, India: a cluster-randomised controlled trial." Lancet **372**(9644): 1151-1162. [PDF Full-Text](#)

**Background** In rural India, most births take place in the home, where high-risk care practices are common. We developed an intervention of behaviour change management, with a focus on prevention of hypothermia, aimed at modifying practices and reducing neonatal mortality. **Methods** We did a cluster-randomised controlled efficacy trial in

Shivgarh, a rural area in Uttar Pradesh. 39 village administrative units (population 104123) were allocated to one of three groups: a control group, which received the usual services of governmental and non-governmental organisations in the area; an intervention group, which received a preventive package of interventions for essential newborn care (birth preparedness, clean delivery and cord care, thermal care [including skin-to-skin care], breastfeeding promotion, and danger sign recognition); or another intervention group, which received the package of essential newborn care plus use of a liquid crystal hypothermia indicator (ThermoSpot). In the intervention clusters, community health workers delivered the packages via collective meetings and two antenatal and two postnatal household visitations. Outcome measures included changes in newborn-care practices and neonatal mortality rate compared with the control group. Analysis was by intention to treat. This study is registered as International Standard Randomised Control Trial, number NCT00198653. Findings Improvements in birth preparedness, hygienic delivery, thermal care (including skin-to-skin care), umbilical cord care, skin care, and breastfeeding were seen in intervention arms. There was little change in care-seeking. Compared with controls, neonatal mortality rate was reduced by 54% in the essential newborn-care intervention (rate ratio 0.46 [95% CI 0.35-0.60],  $p < 0.0001$ ) and by 52% in the essential newborn care plus ThermoSpot arm (0.48 [95% CI 0.35-0.66],  $p < 0.0001$ ). Interpretation A socioculturally contextualised, community-based intervention, targeted at high-risk newborn-care practices, can lead to substantial behavioural modification and reduction in neonatal mortality. This approach can be applied to behaviour change along the continuum of care, harmonise vertical interventions, and build community capacity for sustained development. Funding USAID and Save the Children-US through a grant from the Bill & Melinda Gates Foundation.

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### **Urology**

Menon, M. (2008). "Editorial Comment on: Laparoscopy in German Urology: Changing Acceptance among Urologists." *Eur Urol*. EPub Ahead of Print. [PDF Full-Text](#)

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

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### **Urology**

Menon, M. (2008). "Re: James A. Eastham, Robotic-Assisted Prostatectomy: Is There Truth in Advertising? *Eur Urol* 2008;54:720-2." *Eur Urol*. EPub Ahead of Print. [PDF Full-Text](#)

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

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### **Urology**

Rogers, C. G., A. Metwalli, A. M. Blatt, G. Bratslavsky, M. Menon, W. M. Linehan and P. A. Pinto (2008). "Robotic Partial Nephrectomy for Renal Hilar Tumors: A Multi-Institutional Analysis." *J Urol*. EPub Ahead of Print. *Sladen has an electronic subscription. Issue for this article not available online at the time of this publication.*

Urologic Oncology Branch, National Cancer Institute, National Institutes of Health, Bethesda, Maryland; Vattikuti Urology Institute, Henry Ford Hospital, Detroit, Michigan.

**PURPOSE:** Laparoscopic partial nephrectomy is an advanced surgical procedure requiring technical skill in minimally invasive techniques. Tumors located adjacent to the renal hilum pose an additional challenge. We report a multi-institutional study of robotic partial nephrectomy for renal hilar tumors and describe our results. **MATERIALS AND METHODS:** We evaluated patients from 2 institutions who underwent robotic partial nephrectomy for renal hilar tumors. Renal hilar tumors were defined as tumors abutting the renal artery and/or renal vein on preoperative imaging. After clamping the renal hilar vessels tumors were excised with fine dissection from the renal vessels followed by sutured renal reconstruction. **RESULTS:** Robotic partial nephrectomy was successfully performed on 11 patients (mean age 56.4 years, range 30 to 76). Mean tumor size was 3.8 cm (range 2.3 to 6.4). Mean warm ischemia time was 28.9 minutes (range 20 to 39) and mean operating time was 202 minutes (range 154 to 253). Mean blood loss was 220 ml (range 50 to 750). Mean hospital stay was 2.6 days (range 1 to 4). Histopathological evaluation confirmed 8 cases of clear cell renal cell carcinoma, 1 of papillary renal cell carcinoma and 2 of chromophobe renal cell carcinoma. Surgical margins were negative for malignancy in all cases. **CONCLUSIONS:** Robotic partial nephrectomy is a safe and feasible approach for select patients with renal hilar tumors. Robotic assistance may facilitate tumor resection and renal reconstruction for challenging renal hilar tumors, offering a minimally invasive and nephron sparing surgical option for select patients who might otherwise require open surgery or total nephrectomy.

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