

Henry Ford Health System Publication List September 2009

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

Biostatistics & Research Epidemiology

Joseph, C. L., S. L. Havstad, D. R. Ownby, E. Zoratti, E. L. Peterson, S. Stringer and C. C. Johnson (2009). "Gender differences in the association of overweight and asthma morbidity among urban adolescents with asthma." *Pediatr Allergy Immunol* **20**(4): 362-9. [PDF Full-Text](#)

Henry Ford Health System, Department of Biostatistics & Research Epidemiology, Detroit, MI 48202, USA. cjoseph1@hfhs.org

Asthma and obesity disproportionately affect US African-American youth. Among youth with asthma, obesity has been associated with poor control. The impact of gender on this association is unclear. We examined these relationships in a sample of urban, African-American adolescents with asthma. Questionnaires were used to identify high school students with asthma, and to examine the association of body mass index (BMI) to asthma morbidity, by gender. Of 5967 students completing questionnaires, 599 (10%) met criteria for asthma and 507 had data sufficient for inclusion in further analyses (46% male, mean age = 15.1 yr). Univariately, BMI > 85th percentile was significantly related only to reported emergency department visits (ED) and school days missed for any reason, Odds Ratio (95%Confidence Interval) = 1.7(1.1-2.7), p = 0.01 and 1.8(1.1-3.0), p = 0.01, respectively. A significant gender-BMI interaction (p < 0.05) was observed in multivariate models for ED visits, hospitalizations and school days missed for asthma. In gender-specific models, adjusted Risk Ratios for BMI > 85th and ED visits, hospitalizations, and school days missed because of asthma were 1.7(0.9-3.2), 6.6(3.1-14.6) and 3.6(1.8-7.2) in males. These associations were not observed in females. Gender modifies the association between BMI and asthma-related morbidity among adolescents with asthma. Results have implications for clinical management as well as future research.

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Biostatistics & Research Epidemiology

Wiederkehr, D., K. Berenson, R. Casciano, L. Stern, D. Makenbaeva, E. Mozaffari, L. Lamerato and J. Corbelli (2009). "Clinical impact of early clopidogrel discontinuation following acute myocardial infarction hospitalization or stent implantation: analysis in a single integrated health network." *Current Medical Research and Opinion* **25**(9): 2317-2325.

[Article Request Form](#)

[Wiederkehr, Daniel; Berenson, Karina; Casciano, Roman; Stern, Lee] Analyt Int, New York, NY USA. [Makenbaeva, Dinara] Bristol Myers Squibb Co, Plainsboro, NJ USA. [Mozaffari, Essy] Sanofi Aventis, Bridgewater, NJ USA. [Lamerato, Lois] Henry Ford

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Hlth Syst, Detroit, MI USA. [Corbelli, John] Buffalo Cardiol & Pulm Associates PC, Buffalo, NY USA. [Corbelli, John] SUNY Buffalo, Sch Med & Biomed Sci, Buffalo, NY 14260 USA.
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Objective: To determine the association between the discontinuation of clopidogrel therapy prior to 1 year and the risk of acute myocardial infarction (AMI) hospitalization, coronary intervention or all-cause mortality in a cohort of managed-care patients following AMI hospitalization or stent insertion. **Research design and methods:** This observational cohort study included 1152 patients enrolled in the Health Alliance Plan who were hospitalized for AMI, or who underwent coronary stent placement. Clopidogrel use was assessed using pharmacy claims data. The association between discontinuation of clopidogrel prior to 1 year following the initial ACS event and the primary outcome of AMI hospitalization/procedure was assessed using Cox proportional hazards models. Additionally, an analysis was conducted to determine the association of discontinuation prior to 1 year with a secondary composite outcome of AMI hospitalization/coronary stent procedure or all-cause mortality. **Main outcome measures:** The primary outcome was AMI hospitalization or procedure. The secondary outcome was a composite of AMI hospitalization/procedure, or all-cause mortality. **Results:** Discontinuation of clopidogrel in the total cohort of patients was associated with a significantly higher risk of the primary outcome of AMI hospitalization/coronary intervention (HR 2.712, 95% CI 1.634-4.502). Consistent with this finding, discontinuation of clopidogrel was also associated with a significantly higher risk of the secondary composite endpoint (HR 1.844, 95% CI 1.281-2.653). **Conclusions:** In patients enrolled in an integrated health network, clopidogrel discontinuation prior to 1 year following AMI hospitalization or stent placement is associated with adverse outcomes including greater risk of death, AMI hospitalization or coronary intervention. These results should be interpreted within the context and limitations of observational research, which cannot attribute causality.

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Bone & Joint Center

Yerramshetty, J., D. G. Kim and Y. N. Yeni (2009). "Increased microstructural variability is associated with decreased structural strength but with increased measures of structural ductility in human vertebrae." *J Biomech Eng* **131**(9): 094501. [Article Request Form](#)

Department of Orthopaedics, Bone and Joint Research Center, Henry Ford Hospital, Detroit, MI 48202, USA.

The lack of accuracy in the prediction of vertebral fracture risk from average density measurements, all external factors being equal, may not just be because bone mineral density (BMD) is less than a perfect surrogate for bone strength but also because strength alone may not be sufficient to fully characterize the structural failure of a vertebra. Apart from bone quantity, the regional variation of cancellous architecture would have a role in governing the mechanical properties of vertebrae. In this study, we estimated various microstructural parameters of the vertebral cancellous centrum based on stereological analysis. An earlier study indicated that within-vertebra variability, measured as the coefficient of variation (COV) of bone volume fraction (BV/TV) or as COV of finite element-estimated apparent modulus (E(FE)) correlated well with vertebral strength. Therefore, as an extension to our earlier study, we investigated (i) whether the relationships of vertebral strength found with COV of BV/TV and COV of E(FE) could be extended to the COV of other microstructural parameters and microcomputed tomography-estimated BMD and (ii) whether COV of microstructural parameters were associated with structural ductility measures. COV-based measures were more strongly associated with vertebral strength and ductility measures than average microstructural measures. Moreover, our results support a hypothesis that decreased microstructural variability, while associated with increased strength, may result in decreased structural toughness and ductility. The current findings suggest that variability-based measures could provide an improvement, as a supplement to clinical BMD, in screening for fracture risk through an improved prediction of bone strength and ductility. Further understanding of the biological mechanisms underlying microstructural variability may help develop new treatment strategies for improved structural ductility.

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Cardiology

Harrington, R. A., F. Van de Werf, P. W. Armstrong, P. Aylward, E. Veltri, K. W. Mahaffey, D. J. Moliterno, J. Strony, L. Wallentin, H. D. White, R. Diaz, K. Huber, J. C. Nicolau, J. C. Prieto, D. Isaza, P. Widimsky, P. Grande, M. Nieminen, G. Montalescot, C. Bode, L. Wong, P. Ofner, B. S. Lewis, G. Ambrosio, M. Valgimigli, H. Ogawa, J. Yamaguchi, J. W. Jukema, J. H. Cornel, J. E. Nordrehaug, W. Ruzyllo, L. Providencia, H. C. Tan, A. Dalby, P. Seung-

Jung, A. Betriu, A. Cequier, C. Held, M. Pfisterer, C. Ming-Fong, T. Timurkaynak, R. F. Storey, E. Chen, M. P. Hudson, A. M. Lincoff, D. A. Morrow, P. Tricoci and D. Whellan (2009). "The Thrombin Receptor Antagonist for Clinical Event Reduction in Acute Coronary Syndrome (TRA.CER) trial: study design and rationale." [American Heart Journal](#) **158**(3): 327-U5. [PDF Full-Text](#)

[Harrington, Robert A.; Mahaffey, Kenneth W.; Tricoci, Pierluigi] Duke Clin Res Inst, Durham, NC 27705 USA. [Van de Werf, Frans] Katholieke Univ Leuven, Dept Cardiol, Louvain, Belgium. [Armstrong, Paul W.] Univ Alberta, Div Cardiol, Edmonton, AB, Canada. [Aylward, Phil] Flinders Med Ctr, Dept Cardiovasc Med, Bedford Pk, SA, Australia. [Veltri, Enrico; Strony, John; Chen, Edmond] Schering Plough Corp, Res Inst, Kenilworth, NJ 07033 USA. [Moliterno, David J.] Univ Kentucky, Gill Heart Inst, Lexington, KY USA. [Moliterno, David J.] Univ Kentucky, Div Cardiovasc Med, Lexington, KY USA. [Wallentin, Lars; Held, Claes] Uppsala Clin Res Ctr, Uppsala, Sweden. [White, Harvey D.] Green Lane Cardiovasc Serv, Auckland, New Zealand. [Diaz, Rafael] Inst Cardiovasc Rosario, Rosario, Argentina. [Huber, Kurt] Wilhelminenspital Stadt Wien, Vienna, Austria. [Nicolau, Jose Carlos] Univ Sao Paulo, Sch Med, Heart Inst InCor, BR-05508 Sao Paulo, Brazil. [Carlos Prieto, Juan] Hosp Jose Joaquin Aguirre, Santiago, Chile. [Isaza, Daniel] Fdn Clin Shaio, Bogota, Colombia. [Widimsky, Petr] Univ Hosp Vinohrady, Cardiol, Prague, Czech Republic. [Grande, Peer] Univ Copenhagen Hosp, Ctr Heart, DK-2100 Copenhagen, Denmark. [Nieminen, Markku] Helsinki Univ Cent Hosp, Div Cardiol, Helsinki, Finland. [Montalescot, Gilles] CHU Pitie Salpetriere, Dept Cardiol, Paris, France. [Bode, Christoph] Univ Freiburg Klinikum, Freiburg, Germany. [Wong, Lawrence] Chinese Univ Hong Kong, Div Neurol, Hong Kong, Hong Kong, Peoples R China. [Ofner, Peter] Natl Inst Cardiol, Budapest, Hungary. [Lewis, Basil S.] Heart Hosp, Lady Davis Carmel Med Ctr, Dept Cardiovasc Med, Haifa, Israel. Univ Perugia, Sch Med, Div Cardiol, I-06100 Perugia, Italy. [Valgimigli, Marco] Azienda Osped Univ Ferrara, Cattedra Cardiol, Ferrara, Italy. [Ogawa, Hisao] Kumamoto Univ, Grad Sch Med Sci, Dept Cardiovasc Med, Kumamoto, Japan. [Yamaguchi, Jun-ichi] Tokyo Womens Med Univ, Heart Inst Japan, Dept Cardiol, Tokyo, Japan. [Jukema, J. Wouter] Leiden Univ, Med Ctr, Dept Cardiol, Leiden, Netherlands. [Cornel, Jan H.] Med Ctr Alkmaar, Dept Cardiol, Alkmaar, Netherlands. [Nordrehaug, Jan Erik] Univ Bergen, Bergen, Norway. [Ruzyllo, Witold] Natl Inst Cardiol, Warsaw, Poland. [Providencia, Luis] Hosp Univ Coimbra, Div Cardiol, Coimbra, Portugal. [Tan, Huay-Cheem] Natl Univ Singapore Hosp, Dept Cardiol, Singapore 0511, Singapore. [Dalby, Anthony] Univ Witwatersrand, Johannesburg, South Africa. [Seung-Jung, Park] Asan Med Ctr, Seoul, South Korea. [Betriu, Amadeo] Univ Barcelona, Hosp Clin, Barcelona, Spain. [Cequier, Angel] Univ Barcelona, Bellvitge Hosp, Div Cardiol, Barcelona, Spain. Univ Basel Hosp, Dept Cardiol, CH-4031 Basel, Switzerland. [Ming-Fong, Chen] Natl Taiwan Univ, Coll Med, Taipei 10764, Taiwan. [Timurkaynak, Timur] Gazi Univ Hosp, Dept Cardiol, Ankara, Turkey. [Storey, Robert F.] Univ Sheffield, Cardiovasc Res Unit, Sheffield S10 2TN, S Yorkshire, England. [Hudson, Michael P.] Henry Ford Hosp, Henry Ford Heart & Vasc Inst, Detroit, MI 48202 USA. [Lincoff, A. Michael] Cleveland Clin, Coordinating Ctr Clin Res, Cleveland, OH 44106 USA. [Morrow, David A.] TIMI Study Grp, Boston, MA USA. [Whellan, David] Thomas Jefferson Univ, Div Cardiol, Philadelphia, PA 19107 USA. Tricoci, P, Duke Clin Res Inst, 2400 Pratt St, Room 0311 Terrace Level, Durham, NC 27705 USA. trico001@dcri.duke.edu

Background The protease-activated receptor 1 (PAR-1), the main platelet receptor for thrombin, represents a novel target for treatment of arterial thrombosis, and SCH 530348 is an orally active, selective, competitive PAR-1 antagonist. We designed TRA.CER to evaluate the efficacy and safety of SCH 530348 compared with placebo in addition to standard of care in patients with non-ST-segment elevation (NSTEMI) acute coronary syndromes (ACS) and high-risk features. Trial design TRA.CER is a prospective, randomized, double-blind, multicenter, phase III trial with an original estimated sample size of 10,000 subjects. Our primary objective is to demonstrate that SCH 530348 in addition to standard of care will reduce the incidence of the composite of cardiovascular death, myocardial infarction (MI), stroke, recurrent ischemia with rehospitalization, and urgent coronary revascularization compared with standard of care alone. Our key secondary objective is to determine whether SCH 530348 will reduce the composite of cardiovascular death, MI, or stroke compared with standard of care alone. Secondary objectives related to safety are the composite of moderate and severe GUSTO bleeding and clinically significant TIMI bleeding. The trial will continue until a predetermined minimum number of centrally adjudicated primary and key secondary end point events have occurred and all subjects have participated in the study for at least 1 year. The TRA.CER trial is part of the large phase III SCH 530348 development program that includes a concomitant evaluation in secondary prevention. Conclusion TRA.CER will define efficacy and safety of the novel platelet PAR-1 inhibitor SCH 530348 in the treatment of high-risk patients with NSTEMI ACS in the setting of current treatment strategies. (Am Heart J 2009; 158:327-34.)

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Cardiology

Karthikeyan, V. and K. Ananthasubramaniam (2009). "Coronary risk assessment and management options in chronic kidney disease patients prior to kidney transplantation." Current Cardiology Reviews **5**: 177-86. [Article Request Form](#)

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Cardiology

Sinno, M. C. N., M. Kowalski, D. N. Kenigsberg, S. Khanal and S. C. Krishnan (2009). "Intracoronary electrocardiographic deflections during transmural ischemia induced by percutaneous transluminal coronary angioplasty." Journal of Electrocardiology **42**(5): 453-454. [Article Request Form](#)

[Sinno, Mohamad C. N.; Kowalski, Marcin; Kenigsberg, David N.; Khanal, Sanjaya; Krishnan, Subramaniam C.] Henry Ford Hosp, Detroit, MI 48202 USA.

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Dermatology

Gold, L. F. (2009). "Calcitriol ointment: optimizing psoriasis therapy." J Drugs Dermatol **8**(8 Suppl): s23-7. [PDF Full-Text](#)

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The topical vitamin D3 modulator calcitriol, the naturally occurring active form of vitamin D3, has long been used for topical psoriasis therapy in Europe and other countries and was recently approved in the United States (U.S.) for the treatment of plaque psoriasis. In vehicle-controlled clinical trials, calcitriol 3 microg/g ointment has been shown to significantly improve the symptoms of psoriasis with a low incidence of adverse effects and without affecting calcium homeostasis, even when applied continuously for up to one year. A number of studies have examined the efficacy and safety of calcitriol ointment in combination therapy regimens that also included topical corticosteroid therapy or ultraviolet B (UVB) phototherapy. Calcitriol 3 microg/g ointment is a new option that provides flexibility for use in a variety of psoriasis treatment regimens. According to guidelines developed by the American Academy of Dermatology (AAD), the goals of psoriasis treatment are to produce durable remission of psoriasis symptoms, to achieve "substantial" clearing with the possibility of complete clearing, to maintain the initial benefits of therapy, and to minimize the risk of adverse events. Topical medications are the most commonly used treatments for psoriasis in the U.S. and are important in meeting the goals of psoriasis therapy. These agents offer high response rates with generally favorable safety and tolerability profiles and are useful for both acute treatment and long-term maintenance. Topical medications are used by approximately 85% of patients with psoriasis.

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Dermatology

Mahmoud, B. H. and I. H. Hamzavi (2009). Light treatment of follicular disorders in dark skin. Light-based therapies for skin of color. E. Baron. London, Springer-Verlag.

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Dermatology

Srivastava, D. and D. J. Kouba (2009). "A "Lilliputian" technique for rapid and efficient securing of bolster dressings over full-thickness skin grafts." Dermatol Surg **35**(8): 1280-1. [PDF Full-Text](#)

Department of Dermatology of the Henry Ford Medical Center, Detroit, MI 48202, USA.

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Dermatology

Tierney, E. and D. J. Kouba (2009). "A Subcutaneous Corset Plication Rapidly and Effectively Relieves Tension on Large Linear Closures." [Dermatol Surg EPub Ahead of Print](#). [PDF Full-Text](#)

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

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Dermatology

Tierney, E., B. H. Mahmoud, C. Hexsel, D. Ozog and I. Hamzavi (2009). "Randomized control trial for the treatment of hidradenitis suppurativa with a neodymium-doped yttrium aluminium garnet laser." [Dermatol Surg](#) **35**(8): 1188-98. [PDF Full-Text](#)

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

BACKGROUND: Hidradenitis suppurativa (HS) is a chronic suppurative condition for which there is limited efficacy of medical and surgical treatments. **OBJECTIVE:** To assess whether the 1,064-nm neodymium-doped yttrium aluminium garnet (Nd:YAG) laser is an effective treatment for HS. **MATERIALS AND METHODS:** Prospective, randomized, controlled study for patients with stage II to III HS disease (n=22). A series of 3 monthly laser sessions were performed. Treatment response was measured before each laser session and 1 month after the completion of laser treatment (HS Lesion, Area, and Severity Index (HS-LASI) scale). A modification was made to include symptoms (erythema, edema, pain, and purulent discharge; modified HS-LASI, 0-3 scale). **RESULTS:** The percentage change in HS severity after 3 months of treatment was -65.3% over all anatomic sites, -73.4% inguinal, -62.0% axillary, and -53.1% inframammary. For all anatomic sites combined and each individual anatomic site, the change in HS severity from baseline to month 3 was statistically significant at the treated sites ($p < .02$ for modified HS-LASI and HS-LASI) but not at the control sites ($p > .05$ for modified HS-LASI and HS-LASI). **CONCLUSIONS:** The long-pulse Nd:YAG laser is effective for treatment of HS. The effectiveness of Nd:YAG laser, a hair epilation device, supports the primary follicular pathogenesis of the condition.

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Diagnostic Radiology

Jafari-Khouzani, K., K. Elisevich, S. Patel, B. Smith and H. Soltanian-Zadeh (2009). "FLAIR signal and texture analysis for lateralizing mesial temporal lobe epilepsy." [Neuroimage EPub Ahead of Print](#). [Article Request Form](#)

Department of Diagnostic Radiology, Henry Ford Hospital, Detroit, MI 48202, USA.

Standard magnetic resonance (MR) imaging analysis in several cases of mesial temporal lobe epilepsy (mTLE) either fail to show an identifiable hippocampal asymmetry or provide only subtle distinguishing features that remain inconclusive. A retrospective analysis of hippocampal fluid-attenuated inversion recovery (FLAIR) MR images was performed in cases of mTLE addressing, particularly, the mean and standard deviation of the signal and its texture. Preoperative T1-weighted and FLAIR MR images of 25 nonepileptic control subjects and 36 mTLE patients with Engel class Ia outcomes were analyzed. Patients requiring extraoperative electrocorticography (ECoG) with intracranial electrodes and thus judged to be more challenging were studied as a separate cohort. Hippocampi were manually segmented on T1-weighted images and their outlines were transposed onto FLAIR studies using an affine registration. Image intensity features including mean and standard deviation and wavelet-based texture features were determined for the hippocampal body. The right/left ratios of these features were used with a linear classifier to establish laterality. Whole hippocampal within-subject volume ratios were assessed for comparison. Mean and standard deviation of FLAIR signal intensities lateralized the site of epileptogenicity in 98% of all cases, whereas analysis of wavelet texture features and hippocampal volumetry each yielded correct lateralization in 94% and 83% of cases, respectively. Of patients requiring more intensive study with extraoperative ECoG, 17/18 were lateralized effectively by the combination of mean and standard deviation ratios despite a ratio of mean signal intensity near one in some. The analysis of mean and standard deviation of FLAIR signal intensities provides a highly sensitive method for lateralizing the epileptic focus in mTLE over that of volumetry or texture analysis of the hippocampal body.

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Emergency Medicine

Krishnan, J. A., R. Nowak, S. Q. Davis and M. Schatz (2009). "Anti-Inflammatory Treatment after Discharge Home from the Emergency Department in Adults with Acute Asthma." Journal of Emergency Medicine **37**(2): S35-S41. [PDF Full-Text](#)

[Krishnan, Jerry A.] Univ Chicago, Asthma & COPD Ctr, Pulm & Crit Care Med Sect, Dept Med, Chicago, IL 60637 USA. [Krishnan, Jerry A.] Univ Chicago, Dept Hlth Studies, Chicago, IL 60637 USA. [Nowak, Richard] Henry Ford Hlth Syst, Dept Emergency Med, Detroit, MI USA. [Davis, Steven Q.] Texas Pulm & Crit Care Consultants PA, Ft Worth, TX USA. [Schatz, Michael] Kaiser Permanente Med Ctr, Dept Allergy, San Diego, CA USA.

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Emergency Medicine

Nowak, R., T. Corbridge and B. Brenner (2009). "Noninvasive ventilation." J Allergy Clin Immunol **124**(2 Suppl): S15-8. [PDF Full-Text](#)

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

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Emergency Medicine

Nowak, R., T. Corbridge and B. Brenner (2009). "Noninvasive Ventilation." Journal of Emergency Medicine **37**(2): S18-S22. [PDF Full-Text](#)

[Nowak, Richard] Henry Ford Hlth Syst, Dept Emergency Med, Detroit, MI 48202 USA. [Corbridge, Thomas] Northwestern Univ, Feinberg Sch Med, Div Pulm & Crit Care Med, Chicago, IL 60611 USA. [Brenner, Barry] Univ Hosp, Dept Emergency Med, Case Med Ctr, Case Western Reserve Sch Med, Cleveland, OH USA. Nowak, R, Henry Ford Hlth Syst, Dept Emergency Med, 2799 W Grand Blvd, Detroit, MI 48202 USA.

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Emergency Medicine

Paxton, J. H., T. E. Knuth and H. A. Klausner (2009). "Proximal Humerus Intraosseous Infusion: A Preferred Emergency Venous Access." Journal of Trauma-Injury Infection and Critical Care **67**(3): 606-611. [PDF Full-Text](#)

[Paxton, James H.; Klausner, Howard A.] Henry Ford Hosp, Dept Emergency Med, Detroit, MI 48202 USA. [Knuth, Thomas E.] Henry Ford Hosp, Dept Surg, Div Acute Care Surg, Detroit, MI 48202 USA. Paxton, JH, Henry Ford Hosp, Dept Emergency Med, 2799 W Grand Blvd, Detroit, MI 48202 USA. jpaxton1@hfhs.org

Purpose: To assess the proximal humerus intraosseous (PHIO) catheter placement as a preferred method for venous access over conventional methods, including peripheral intravenous (PIV) and central venous catheters (CVCs), during emergency room resuscitation. Methods: In phase 1, conventional methods for venous access (PIV and CVC) were assessed for all patients presenting to the emergency department resuscitation bay. Outcome measures in both phases were speed, immediate complications, and pain. CVC placement was performed when PIV access was deemed impossible or when rapid volume resuscitation was needed. In phase 2, resuscitations requiring venous access or complicated by failed PIV access attempts underwent PHIO catheter placement. Results: Sixty-two patients received either PIV (57) or CVC (5) catheterization, and 29 patients received 30 PHIO catheters. PHIO catheter placement was significantly faster than conventional methods (1.5 [SD 1.1] versus 3.6 minutes [SD 3.7; $p < 0.001$ for PIV, and 15.6 minutes [SD 6.7; $p < 0.0056$] for CVC). No major complications were identified in either phase. Minor complications for PIV access included extravasation and placement failure. Minor complications for CVC placement included inability to thread the guidewire. Minor complications with PHIO catheter placement included placement failure, poor flow, and catheter dislodgement. Pain scores associated with PHIO insertion and infusion were higher than those associated with PIV and CVC catheter placement. Conclusion: PHIO catheter placement is significantly

faster than PIV and CVC placement with increased minor complication profile and perceived pain. PHIO venous access is absolutely life saving when PIV or CVC placement is difficult or impossible.

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Emergency Medicine

Schatz, M., A. N. Kazzi, B. Brenner, C. A. Camargo, T. Corbridge, J. A. Krishnan, R. Nowak and G. Rachelefsky (2009). "Introduction." Journal of Emergency Medicine **37**(2): S1-S5. [PDF Full-Text](#)

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Endocrinology & Metabolism

Benjamin, A., A. Moriakova, N. Akhter, D. Rao, H. Xie, S. Kukreja and E. Barengolts (2009). "Determinants of 25-hydroxyvitamin D levels in African-American and Caucasian male veterans." Osteoporosis International **20**(10): 1795-1803. [PDF Full-Text](#)

[Benjamin, A.; Moriakova, A.; Akhter, N.; Kukreja, S.; Barengolts, E.] Univ Illinois, Med Ctr, Dept Med, Sect Endocrinol & Metab, Chicago, IL 60612 USA. [Xie, H.] Univ Illinois, Med Ctr, Div Epidemiol & Biostat, Chicago, IL 60612 USA. [Rao, D.] Henry Ford Hosp, Bone & Mineral Res Lab, Detroit, MI 48202 USA. Barengolts, E, Univ Illinois, Med Ctr, Dept Med, Sect Endocrinol & Metab, MC 640, 1819 W Polk St, Chicago, IL 60612 USA. eibareng@uic.edu

Among 307 males seen in VA Medical Center, independent determinants ($p < 0.01$ for all) of serum 25-hydroxyvitamin D [25(OH)D] levels included race, vitamin D supplements, BMI, dietary calcium intake and smoking, but not age. Negative association between 25(OH)D and parathyroid hormone (PTH) was similar for Caucasian and African-American men. In this prospective cohort study, we examined determinants of serum 25-hydroxyvitamin D [25(OH)D] levels and the relationship between 25(OH)D and PTH levels and body mass index (BMI). Male veterans ($n = 307$) were recruited at a VA Medical Center. Serum levels of PTH and 25(OH)D were obtained. Surveys and chart reviews were completed. Vitamin D insufficiency was defined as 25(OH)D < 30 ng/ml. Univariate and multivariate regression analyses were performed. Among 232 African-American (AA) men (mean \pm SD), 25(OH)D level (21.4 ± 10.4 ng/ml) was lower and prevalence of insufficiency (80%) was higher than among 75 Caucasians (C; 28.5 ± 11.1 ng/ml and 53%, respectively, $p < 0.01$ for both). In multivariate regression analysis, independent determinants ($p < 0.01$ for all) of 25(OH)D levels included AA race, vitamin D supplements, BMI, dietary calcium intake, and smoking. Despite lower 25(OH)D levels in African-Americans, PTH levels were similar to those seen in Caucasians. There was a significant ($p < 0.02$) negative linear association between 25(OH)D and PTH in African-American ($r(2) = 0.05$) and Caucasian ($r(2) = 0.08$) men, and there was no difference between the slopes of the relationship. 25(OH)D levels are determined by modifiable risk factors such as vitamin D supplementation in both AA and C males. The negative association between 25(OH)D and PTH is similar between the two races.

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Eye Care Services

Guo, A. M., G. Scicli, J. Sheng, J. C. Falck, P. A. Edwards and A. G. Scicli (2009). "20-HETE can act as a nonhypoxic regulator of HIF-1alpha in human microvascular endothelial cells." Am J Physiol Heart Circ Physiol **297**(2): H602-13. [PDF Full-Text](#)

20-HETE increases the expression of VEGF in human dermal microvascular endothelial cells (ECs). Since VEGF is regulated by hypoxia inducible factor (HIF)-1, we studied whether 20-HETE also upregulates HIF-1 α using the stable 20-HETE analog 20-hydroxyeicosa-5(Z),14(Z)dienoic acid (WIT003; 1-10 μ M) and found that it induced a marked increase in HIF-1 α protein levels. The increases in VEGF after the addition of WIT003 preceded the changes in HIF-1 α , and the increases in HIF-1 α were prevented by a VEGF neutralizing antibody. This suggests that 20-HETE first causes increases in VEGF, which then, in turn, cause the upregulation of HIF-1 α . Stimulation with exogenously added VEGF also led to an upregulation of HIF-1 α . Incubation with the MEK1/ERK1/2 inhibitor U-0126 (10 μ M) completely abolished the increases in VEGF and thus HIF-1 α , suggesting the involvement of ERK1/2 activation. The addition of WIT003 resulted in a rapid and sustained increase in superoxide formation. When WIT003 was added in the presence of the nitric oxide (NO) synthase (NOS) inhibitor N-nitro-L-arginine, no changes in superoxide, VEGF, or HIF-1 α were observed. This suggests that NOS is responsible for the early changes in superoxide induced by WIT003. Furthermore, WIT003 induced the expression of the NADPH oxidase subunit p47(phox) in ECs before the increases in HIF-1 α . Incubation with polyethylene glycol-superoxide dismutase (400 U/ml), apocynin (100 μ M), diphenylene iodonium (10 μ M), or p47(phox) downregulation with small interfering (si)RNA all inhibited the increases in HIF-1 α expression. This indicates that the early changes in superoxide lead to VEGF increases and thereby NADPH oxidase-dependent superoxide production, which is required for HIF-1 α upregulation. We also found that the higher HIF-1 α expression induced by WIT003 was accompanied by higher expression of erythropoietin receptor and angiopoietin-2 proteins. These increases were caused by HIF-1 α because their levels were markedly decreased by siRNA downregulation of HIF-1 α . 20-HETE may be a novel nonhypoxic regulator of HIF-1 α and HIF-1 α -regulated genes in ECs.

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Hematology, Medical Oncology & Josephine Ford Cancer Center

Whitehead, R. P., C. Rankin, P. M. G. Hoff, P. J. Gold, K. G. Billingsley, R. A. Chapman, L. Wong, J. H. Ward, J. L. Abbruzzese and C. D. Blanke (2009). "Phase II trial of romidepsin (NSC-630176) in previously treated colorectal cancer patients with advanced disease: a Southwest Oncology Group study (S0336)." *Investigational New Drugs* **27**(5): 469-475.

[PDF Full-Text](#)

[Whitehead, Robert P.] Med Univ S Carolina, Charleston, SC 29425 USA. [Rankin, Cathryn] SW Oncol Grp, Ctr Stat, Seattle, WA USA. [Hoff, Paulo M. G.] Inst Canc Sao Paulo, Sao Paulo, Brazil. [Gold, Philip J.] Swedish Canc Inst, Seattle, WA USA. [Billingsley, Kevin G.] Oregon Hlth & Sci Univ, Portland, OR 97201 USA. [Chapman, Robert A.] Henry Ford Hosp, Detroit, MI 48202 USA. [Wong, Lucas] Scott & White Mem Hosp & Clin, Temple, TX USA. [Ward, John H.] Univ Utah, Hlth Sci Ctr, Salt Lake City, UT USA. [Abbruzzese, James L.] Univ Texas Houston, MD Anderson Canc Ctr, Houston, TX 77030 USA. [Blanke, Charles D.] Univ British Columbia, Vancouver, BC V5Z 1M9, Canada.

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Introduction: Patients with metastatic colorectal cancer who progress on standard chemotherapy have limited treatment options. New and effective drugs are needed for these patients. Romidepsin is a histone deacetylase inhibitor that can alter chromatin structure and gene transcription leading to multiple changes in cellular protein production. This may result in cell cycle arrest and tumor growth inhibition. Romidepsin has shown anti-proliferative activity in vitro against multiple mouse and human tumor cell lines and in vivo in human tumor xenograft models. Patients and methods: Patients were required to have pathologically verified, measurable, metastatic or locally advanced colorectal cancer that was surgically unresectable. They must have failed either one or two prior chemotherapy regimens, had performance status of 0-1, adequate bone marrow, renal and hepatic function, and no significant cardiac disease. Patients were treated with romidepsin at a dose of 13 mg/m² as a 4-h iv infusion on days 1, 8, and 15 of a 28-day cycle. The study had a two stage design. The primary objective of the study was to determine the confirmed response probability in this group of patients treated with romidepsin. Results: Twenty-eight patients were registered to the study, two of whom were ineligible. One eligible patient refused all treatment and was not analyzed. For the 25 remaining patients, performance status was 0 in 16 patients and 1 in nine patients. Ten patients had received one prior chemotherapy regimen and fifteen 2 prior regimens. Out of the 25 eligible and analyzable patients accrued in the first stage of the protocol, no objective responses were observed and the study was permanently closed. Four patients had stable disease as the best response. Twenty-five patients were assessed for toxicity. No

grade 4 or greater toxicities were seen. Fourteen of the 25 patients experienced grade 3 toxicities the most common of which were fatigue or anorexia. Conclusion: Romidepsin at this dose and schedule is ineffective in the treatment of patients with metastatic colorectal cancer after prior chemotherapy. Future trials might evaluate combinations of romidepsin with chemotherapeutic or other agents.

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Hypertension & Vascular Research

Caceres, P. S., G. R. Ares and P. A. Ortiz (2009). "cAMP Stimulates Apical Exocytosis of the Renal Na⁺-K⁺-2Cl⁻ Cotransporter NKCC2 in the Thick Ascending Limb ROLE OF PROTEIN KINASE A." Journal of Biological Chemistry **284**(37): 24965-24971. [PDF Full-Text](#)

[Caceres, Paulo S.; Ares, Gustavo R.; Ortiz, Pablo A.] Henry Ford Hosp, Hypertens & Vasc Res Div, Detroit, MI 48202 USA. [Caceres, Paulo S.; Ortiz, Pablo A.] Wayne State Univ, Sch Med, Dept Physiol, Detroit, MI 48202 USA.

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The apical renal Na⁺-K⁺-2Cl⁻ cotransporter NKCC2 mediates NaCl absorption by the thick ascending limb (TAL) of Henle's loop. cAMP stimulates NKCC2 by enhancing steady-state apical membrane levels of this protein; however, the trafficking and signaling mechanisms by which this occurs have not been studied. Here, we report that stimulation of endogenous cAMP levels with either forskolin/3-isobutyl-1-methylxanthine (IBMX) or the V2 receptor agonist [deamino-Cys(1),D-Arg(8)] vasopressin increases steady-state surface NKCC2 and that the protein kinase A (PKA) inhibitor H-89 blocks this effect. Confocal imaging of apical surface NKCC2 in isolated perfused TALs confirmed a stimulatory effect of cAMP on apical trafficking that was blocked by PKA inhibition. Selective stimulation of PKA with the agonist N-6-benzoyl-cAMP (500 μM) stimulated steady-state surface NKCC2, whereas the Epac-selective agonist 8-p-chlorophenylthio-2'-O-methyl-cAMP (100 and 250 μM) had no effect. To explore the trafficking mechanism by which cAMP increases apical NKCC2, we measured cumulative apical membrane exocytosis and NKCC2 exocytic insertion in TALs. By monitoring apical FM1-43 fluorescence, we observed rapid stimulation of apical exocytosis (2 min) by forskolin/IBMX. We also found constitutive exocytic insertion of NKCC2 in TALs over time, which was increased by 3-fold in the presence of forskolin/IBMX. PKA inhibition blunted cAMP-stimulated exocytic insertion but did not affect the rate of constitutive exocytosis. We conclude that cAMP stimulates steady-state apical surface NKCC2 by stimulating exocytic insertion and that this process is highly dependent on PKA but not Epac.

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Hypertension & Vascular Research

Li, X. C., Y. Shao and J. L. Zhuo (2009). "AT1a receptor knockout in mice impairs urine concentration by reducing basal vasopressin levels and its receptor signaling proteins in the inner medulla." Kidney Int **76**(2): 169-77. [PDF Full-Text](#)

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

in the knockout mice. We suggest that AT(1a) receptor deletion causes polyuria and urine concentration defects by decreasing basal AVP release and impairing AVP-induced receptor signaling in the inner medulla.

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Hypertension & Vascular Research

Ortiz-Capisano, M. C., T. D. Liao, P. A. Ortiz and W. H. Beierwaltes (2009). "Calcium-dependent phosphodiesterase 1C inhibits renin release from isolated juxtaglomerular cells." Am J Physiol Regul Integr Comp Physiol **Epub Ahead of Print**. [PDF Full-Text](#)

Henry Ford Hospital.

Renin release from the juxtaglomerular (JG) cell is stimulated by the second messenger cAMP and inhibited by calcium. We previously showed JG cells contain a calcium sensing receptor (CaSR) which, when stimulated, decrease cAMP formation and inhibit renin release. We hypothesize CaSR activation decreases cAMP and renin release in part by stimulating a calcium-calmodulin activated phosphodiesterase 1 (PDE1). We incubated our primary culture of JG cells with two selective PDE1 inhibitors (8-MM-IBMX (20 microM) and Vinpocetine (40 microM)) and the calmodulin inhibitor W-7 (10 microM) and measured cAMP and renin release. Stimulation of the JG cell CaSR with the calcimimetic Cinacalcet (1 microM) resulted in decreased cAMP from basal of 1.13 +/- 0.14 to 0.69 +/- 0.08 pM/mg protein ($p < 0.001$) and in renin release from 0.89 +/- 0.16 to 0.38 +/- 0.08 microgANGI/ml/hr/mg protein ($p < 0.001$). However, the addition of 8-MM-IBMX with Cinacalcet returned both cAMP (1.10 +/- 0.19 pM/mg protein) and renin (0.57 +/- 0.16 microgANGI/ml/hr/mg protein) to basal levels. Similar results were obtained with Vinpocetine, and also with W-7. Combining 8-MM-IBMX and W-7 had no additive effect. To determine which PDE1 isoform is involved, we performed Western blots for PDE1A, B and C. Only Western blot for PDE1C showed a characteristic band apparent at 80 kDa. Immunofluorescence showed cytoplasmic distribution of PDE1C and renin in the JG cells. In conclusion, PDE1C is expressed in isolated JG cells, and contributes to calcium's inhibitory modulation of renin release from JG cells. Key words: renin, calcium, phosphodiesterase, calmodulin.

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Hypertension & Vascular Research

Silva, G. B. and J. L. Garvin (2009). "Akt1 mediates purinergic-dependent NOS3 activation in thick ascending limbs." Am J Physiol Renal Physiol **297(3)**: F646-52. PMC2739713. [Article Request Form](#)

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Extracellular ATP regulates many physiological processes via release of nitric oxide (NO). ATP stimulates NO in thick ascending limbs (TALs), but the signaling cascade involved in the cells of this nephron segment, as well as many other types of cells, is poorly understood. We hypothesized that ATP enhances NO synthase (NOS) activity by stimulating PI3 kinase and Akt. We measured 1) NO in TALs using the NO-sensitive dye DAF-2 DA and 2) Akt activity by fluorescence resonance energy transfer and phosphorylation of Akt isoforms. ATP (100 microM) stimulated NO in wild-type mice [26 +/- 4 arbitrary units (AU)], but not in NOS3 -/- mice (2 +/- 2 AU; $P < 0.04$). In the presence of the NOS1- and NOS2-selective inhibitors 7-NI and 1400W, ATP stimulated NO by 30 +/- 2 and 33 +/- 3 AU, respectively (not significant vs. control). In the presence of the PI3 kinase inhibitor LY294002, ATP-increased NO was reduced by 85% (5 +/- 2 vs. 28 +/- 4 AU; $P < 0.02$). ATP alone increased Akt activity and this effect was significantly blocked by suramin, a P2 receptor antagonist. In the presence of an Akt-selective inhibitor, ATP-induced NO was blocked by 90 +/- 4%. ATP significantly stimulated Akt1 phosphorylation at Ser(473) by 91 +/- 13%, whereas Akt2 phosphorylation remained unchanged and Akt3 phosphorylation decreased. In vivo transduction of TALs with a dominant-negative Akt1 significantly decreased ATP-induced NO by 88 +/- 6%. We concluded that ATP increases NOS3-derived NO via Akt1 activation in the TAL.

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Internal Medicine

Arabi, Z. and A. Boxwalla (2009). "Repeated Stool Toxin Testing for Diagnosing Difficile Colitis Is Still Valid." South Med J **Epub Ahead of Print**. [PDF Full-Text](#)

From the Departments of Internal Medicine and Infectious Diseases, Henry Ford Hospital, Detroit, MI.

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Internal Medicine

Yan, B., A. M. Noone, C. Yee, M. Banerjee, K. Schwartz and M. S. Simon (2009). "Racial differences in colorectal cancer survival in the Detroit Metropolitan Area." Cancer **115**(16): 3791-800. [PDF Full-Text](#)

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

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Nephrology

Besarab, A., W. H. Horl and D. Silverberg (2009). "Iron metabolism, iron deficiency, thrombocytosis, and the cardiorenal anemia syndrome." Oncologist **14 Suppl 1**: 22-33. [Article Request Form](#)

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

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Nephrology

Moore, C., J. Yee, H. Malluche, D. S. Rao, M. C. Monier-Faugere, E. Adams, O. Daramola-Gunwuyi, H. Fehmi, S. Bhat and Y. Osman-Malik (2009). "Relationship between Bone Histology and Markers of Bone and Mineral Metabolism in African-American Hemodialysis

Patients." Clinical Journal of the American Society of Nephrology 4(9): 1484-1493. [Article Request Form](#)

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Background and objectives: Racial differences in mineral metabolism exist in the chronic kidney disease population, especially as it relates to intact parathyroid hormone (iPTH) levels. Few data exist on the relationship of these markers to bone biopsy findings in African-American (AA) hemodialysis patients across the spectrum of renal osteodystrophy (ROD). Design, setting, participants, & measurements: In prevalent AA hemodialysis subjects, we prospectively evaluated subjects by performing transiliac bone biopsy and correlating biochemical and clinical data to bone histology. Results: Study patients (n = 43) had an average age of 53.7 (+/-11.6) yr, with dialysis vintage of 40.4 (+/-24.5) mo, 30% with diabetes, and 51% male. Bone histology revealed adynamic bone disease (ABD) (16%), mild to moderate hyperparathyroidism (HPT) (72%), severe (12%) HPT, and no osteomalacia or mixed uremic osteodystrophy. At the time of biopsy, mean corrected calcium was 9.1, 8.9, and 9.4 mg/dl (P = 0.344); calcium-phosphorus (Ca x PO₄) product was 42, 55, and 62 mg(2)/dl(2) (P = 0.002); phosphorus was 4.6, 6.2, and 6.7 mg/dl (P = 0.005); and iPTH was 225, 566, and 975 pg/ml (P = 0.006), respectively. Median values for bone-specific alkaline phosphatase (BS-AP) were 16, 34, and 64 ng/ml (P < 0.0001) among the three groups. Conclusions: These data demonstrate that across the spectrum of ROD, iPTH levels are higher than expected in AA hemodialysis subjects. iPTH, PTH peptides, and bone-specific alkaline phosphatase correlated directly with histomorphometric measurements of bone turnover and when subjects were grouped by histologic diagnosis. Only 9.5% of subjects were simultaneously within suggested Kidney Disease Outcomes Quality Initiative (K/DOQI) ranges for Ca x PO₄, phosphorus, and iPTH, of which 75% demonstrated ABD on biopsy. Clin J Am Soc Nephrol 4: 1484-1493, 2009. doi: 10.2215/CJN.01770408

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Neurology

Cerghet, M., L. Schultz, J. Elston-Lafata, R. Salloum, E. Dobie and S. Elias (2009). "Employment, quality of life and exposure to disease-modifying agents among patients with multiple sclerosis: a multi-year analysis." Multiple Sclerosis 15(9): S56-S56. [Article Request Form](#)

[Cerghet, M.; Schultz, L.; Elston-Lafata, J.; Salloum, R.; Dobie, E.; Elias, S.] Henry Ford Hosp, Detroit, MI 48202 USA.

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Neurology

Chen, J., A. Zacharek, X. Cui, A. Shehadah, H. Jiang, C. Roberts, M. Lu and M. Chopp (2009). "Treatment of stroke with a synthetic liver X receptor agonist, TO901317, promotes synaptic plasticity and axonal regeneration in mice." J Cereb Blood Flow Metab **Epub Ahead of Print**. [Article Request Form](#)

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

In this study, we tested the hypothesis that TO901317 promotes synapse plasticity and axonal regeneration after stroke. Adult male C57BL/6J mice were subjected to middle cerebral artery occlusion (MCAo) and treated with or without TO901317 starting 24 h after MCAo daily for 14 days. Axonal damage and regeneration were evaluated by immunostaining. TO901317 significantly increased synaptophysin expression and axonal regeneration, as well as decreased the expressions of amyloid betaA4 precursor protein and Nogo receptor (NgR) in the ischemic brain. To test whether TO901317 regulates the phosphorylation of phosphatidylinositol 3-kinase (p-PI3K) and Akt (p-Akt) activity in the ischemic brain, MCAo mice were treated with or without TO901317 starting 24 h after MCAo daily for 4 days and were then killed at 5 days after MCAo. TO901317

treatment significantly increased p-PI3K and p-Akt activity, but did not increase total PI3K expression in the ischemic brain. Using primary cortical neuron (PCN) culture, TO901317 significantly increased synaptophysin expression, p-PI3K activity, and decreased NgR expression compared with nontreated controls. TO901317 also significantly increased neurite outgrowth, and inhibition of the PI3K/Akt pathway by LY294002 decreased neurite outgrowth in both controls and TO901317-treated groups in cultured hypoxic PCN. These data indicate that TO901317 promotes synaptic plasticity and axonal regeneration, and that PI3K/Akt signaling activity contributes to neurite outgrowth. *Journal of Cerebral Blood Flow & Metabolism* advance online publication, 2 September 2009; doi:10.1038/jcbfm.2009.187.

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Neurology

Katakowski, M., F. Jiang, X. Zheng, J. A. Gutierrez, A. Szalad and M. Chopp (2009). "Tumorigenicity of cortical astrocyte cell line induced by the protease ADAM17." *Cancer Sci* **100**(9): 1597-604. PMC2756136. [PDF Full-Text](#)

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

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Neurology

Schuh, L. A., Z. London, R. Neel, C. Brock, B. M. Kissela, L. Schultz and D. J. Gelb (2009). "Education Research: Bias and poor interrater reliability in evaluating the neurology clinical skills examination." *Neurology* **73**(11): 904-908. [PDF Full-Text](#)

[Schuh, L. A.] Henry Ford Hosp, Dept Neurol, Detroit, MI 48202 USA. [Schultz, L.] Henry Ford Hosp, Dept Biostat & Res Epidemiol, Detroit, MI 48202 USA. [London, Z.; Gelb, D. J.] Univ Michigan, Sch Med, Dept Neurol, Ann Arbor, MI USA. [Neel, R.; Kissela, B. M.] Univ Cincinnati, Dept Neurol, Cincinnati, OH 45221 USA. [Brock, C.] Univ S Florida, Dept Neurol, Tampa, FL 33620 USA.

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

bias was detected for favorable assessment locally, which is concerning for the validity of the examination. Further study is needed to assess whether training can improve interrater reliability and offset bias. *Neurology* (R) 2009;73:904-908

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Neurology

Senderek, J., S. M. Garvey, M. Krieger, I. Tournev, M. Elbracht, A. Roos, C. Stendel, A. Urtizbera, V. Guergueltcheva, V. Mihailova, H. Feit, J. Tramonte, P. Hedera, C. Bergmann, S. Rudnik-Schoneborn, K. Zerres, H. Lochmuller, E. Seboun, J. S. Beckmann, M. A. Hauser, C. E. Jackson and J. Weis (2009). "A new autosomal dominant distal vacuolar myopathy associated with mutation of the nuclear matrix protein, matrin 3." *Neuromuscular Disorders* **19**(8-9): 599-599. [Article Request Form](#)

[Senderek, J.; Stendel, C.] ETH, Inst Cell Biol, CH-8093 Zurich, Switzerland. [Garvey, S. M.] Univ Virginia, Robert M Berne Cardiovasc Res Ctr, Charlottesville, VA USA. [Krieger, M.; Elbracht, M.; Roos, A.; Bergmann, C.; Rudnik-Schoeneborn, S.; Zerres, K.] Univ Aachen, Rhein Westfal TH Aachen, Inst Human Genet, D-5100 Aachen, Germany. [Tournev, I.; Guergueltcheva, V.; Mihailova, V.] Med Univ Sofia, Mol Med Ctr, Sofia, Bulgaria. [Urtizbera, A.] Hop Martin de Hendaye, Hendaye, France. [Feit, H.] Henry Ford Hosp, Dept Neurol, Detroit, MI 48202 USA. [Tramonte, J.] Scott & White Mem Hosp & Clin, Dept Neurol, Temple, TX 76508 USA. [Hedera, P.] Vanderbilt Univ, Dept Neurol, Nashville, TN USA. [Lochmueller, H.] Inst Human Genet, Newcastle Upon Tyne, Tyne & Wear, England. [Seboun, E.] Univ Paris 06, Div Genet & Microbiol, Paris, France. [Beckmann, J. S.] Univ Lausanne, Lausanne, Switzerland. [Beckmann, J. S.] CHU Vaudois, Dept & Serv Med Genet, CH-1011 Lausanne, Switzerland. [Hauser, M. A.] Duke Univ, Med Ctr, Ctr Human Genet, Durham, NC USA. [Jackson, C. E.] Scott & White Mem Hosp & Clin, Dept Med, Temple, TX 76508 USA. [Weis, J.] Univ Aachen, Rhein Westfal TH Aachen, Inst Neuropathol, Aachen, Germany.

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Neurology

Silver, B., S. McCarthy, M. Lu, P. Mitsias, A. N. Russman, A. Katramados, D. C. Morris, C. A. Lewandowski and M. Chopp (2009). "Sildenafil Treatment of Subacute Ischemic Stroke: A Safety Study at 25-mg Daily for 2 Weeks." *Journal of Stroke & Cerebrovascular Diseases* **18**(5): 381-383. [Article Request Form](#)

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Background: In several animal studies of young and aged rats with ischemic stroke, treatment with sildenafil improved functional outcomes compared with placebo. We conducted a safety study of sildenafil (25 mg daily for 2 weeks) shortly after ischemic stroke onset. Methods: We recruited patients aged 18 to 80 years with ischemic stroke, National Institutes of Health stroke scale (NIHSS) score 2 to 21, between days 2 and 9 after symptom onset. Patients were treated with sildenafil for 2 weeks (25 mg daily). The primary outcome measure was the adverse occurrence of any of the following during the treatment period: stroke worsening, new stroke, myocardial infarction, vision loss, hearing loss, or death from any cause. Secondary outcome measures were NIHSS score, Barthel indices, and modified Rankin score at 90 days. Results: Twelve patients were recruited. Mean age was 57 years, 5 were female, and median NIHSS score at entry was 9.5 (range 2-20). The primary outcome measure occurred in one patient (sudden death). Another patient committed suicide 2 months after study entry (and 6 weeks after treatment with sildenafil had been completed). Among the 10 survivors, at 90 days, median NIHSS score was 2 (range 0-12), median Barthel index was 95 (range 15-100), and median modified Rankin score was 1.5 (range 0-5). Conclusions: Sildenafil (25 mg daily for 2 weeks) appeared to be safe in this group of patients with mild to moderately severe stroke. Further studies of higher doses will be tested.

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Neurology

Zhang, X., X. Zheng, F. Jiang, Z. G. Zhang, M. Katakowski and M. Chopp (2009). "Dual-color fluorescence imaging in a nude mouse orthotopic glioma model." J Neurosci Methods **181**(2): 178-85. PMC2738429. [Article Request Form](#)

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

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Neurosurgery

Krishnamurthy, S., A. Navarro-Martin and A. Maitz (2009). "Gamma Knife radiosurgery for occipital condyle metastasis." Clin Transl Oncol **11**(9): 622-4. [PDF Full-Text](#)

Department of Neurological Surgery, Henry Ford Hospital, Detroit, MI, USA.

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

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Neurosurgery

Nerenz, D. R. (2009). "Ethical issues in using data from quality management programs." European Spine Journal **18**: S321-S330. [PDF Full-Text](#)

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

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Neurosurgery

Xiong, Y., A. Mahmood, C. Qu, H. Kazmi, Z. G. Zhang, C. Noguchi, T. Schallert and M. Chopp (2009). "Erythropoietin improves histological and functional outcomes following

traumatic brain injury in mice in the absence of the neural erythropoietin receptor." [J Neurotrauma EPub Ahead of Print. Article Request Form](#)

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Erythropoietin (EPO), essential for erythropoiesis, provides neuroprotection. The EPO receptor (EPOR) is expressed in both neural and non-neural cells in the brain. This study was designed to test the hypothesis that EPO provides beneficial therapeutic effects even in the absence of the neural EPOR. In this study, EPOR-null mice were rescued with selective EpoR expression driven by the endogenous EpoR promoter in hematopoietic tissue but not in the neural cells. Anesthetized young adult female EPOR-null and wild-type mice were subjected to traumatic brain injury (TBI) induced by controlled cortical impact. EPO (5000 U/kg) or saline was intraperitoneally administered at 6 h, and 3 and 7 days post injury. Sensorimotor and spatial learning functions were assessed. Expression of EPOR and its downstream signal proteins were evaluated by Western blot analysis. Our data demonstrated that EPO treatment significantly reduced cortical tissue damage and hippocampal cell loss, and improved spatial learning following TBI in both the wild-type and EPOR-null mice. EPO treatment significantly improved sensorimotor functional recovery, with better outcomes in the wild-type mice. EPO treatment upregulated antiapoptotic proteins (p-Akt and Bcl-XL) in the ipsilateral hippocampus and cortex of the injured wild-type and EPOR-null mice. These data demonstrate that EPO significantly provides neuroprotection following TBI even in the absence of EPOR in the neural cells, suggesting that its therapeutic benefits may be mediated through vascular protection.

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Other

Baylis, J., R. Burks, J. L. Colletta, P. M. Cooley, J. Flores, M. Goldstein, M. Hendricks, D. D. Peabody, T. G. Peters, E. M. Power, C. L. Russell, T. Sebers, S. M. Torrence, A. W. Webb, N. Weimert and C. Goodman (2009). "Defining high risk in adult kidney transplantation." [Progress in Transplantation](#) **19**(3): 252-258. [Article Request Form](#)

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Background-Because identifiable factors contribute to allograft loss, and because no consensus has been reached on the definition of high risk, an interdisciplinary group of nurses, physicians, pharmacists, and social workers was convened in May 2008. Objective-Participants sought to reach consensus about the current state of science and best practices related to the definition and management of high-risk kidney transplant recipients. Methods-An expert facilitator with extensive experience in leading consensus teams guided consensus-building activities, which included discussion and small-group work. Results-This consensus group conceptualized the definition of the "high-risk" kidney transplant recipient and provided information to guide the multidisciplinary team in their assessment of these patients before and after transplant. Three key areas, which were conceptualized as independent scales, had a substantial impact on outcomes: (1) transplant recipient medical factors, (2) donor and recipient immunological factors, and (3) transplant recipient psychosocial factors. Though depicted separately, alteration of a specific risk on one scale could influence some risk factors on another scale. In addition, the kidney allograft itself must be considered in the assessment of high risk. Conclusions-The continuum of risk described here should be useful to transplant clinicians in their assessment of high-risk adult kidney transplant patients, may aid centers in developing a more complete definition of high risk, and may lead to risk-reduction efforts. ([Progress in Transplantation](#). 2009; 19:252-258)

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Other

Brown, A. R., P. Coppola, M. Giacona, A. Petriches and M. A. Stockwell (2009). "Faith community nursing demonstrates good stewardship of community benefit dollars through cost savings and cost avoidance." Fam Community Health **32**(4): 330-8. [PDF Full-Text](#)

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

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Otolaryngology

Ghanem, T. A. and M. K. Wax (2009). "A novel split-thickness skin graft donor site: The radial skin paddle." Otolaryngology-Head and Neck Surgery **141**(3): 390-394. [PDF Full-Text](#)

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OBJECTIVE: To eliminate morbidity of the thigh split-thickness skin graft (STSG) donor site in forearm flaps, the feasibility of harvesting from an alternate site was assessed. **STUDY DESIGN:** Case series with planned data collection. **SETTING:** A tertiary care academic setting. **SUBJECTS AND METHODS:** Data were collected from patients undergoing forearm flap reconstruction over 13 months. The forearm flap harvesting procedure was modified to incorporate STSG harvest directly from the flap skin paddle. **RESULTS:** There were 66 patients in this cohort, with mean age of 62.6 years. There were 58 fasciocutaneous radial forearm free flaps (RFFFs), three osteocutaneous RFFF, three ulnar flaps, and two reverse-flow RFFFs. The majority of flaps were used for mucosal coverage (n = 54), but 12 flaps were used for external skin coverage. The mean forearm defect was 36.5 cm(2) (12-77 cm(2)). Harvesting from the forearm skin paddle was successful in 64 patients (97%). Two patients required a thigh STSG; both patients were octogenarians with frail skin. **CONCLUSION:** A thigh STSG donor site, with its associated morbidities, can be eliminated in 97 percent of patients undergoing forearm flaps. Older patients with frail skin may require a thigh donor site. (C) 2009 American Academy of Otolaryngology-Head and Neck Surgery Foundation. All rights reserved.

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Otolaryngology

Schwartz, S. R., S. M. Cohen, S. H. Dailey, R. M. Rosenfeld, E. S. Deutsch, M. B. Gillespie, E. Granieri, E. R. Hapner, C. E. Kimball, H. J. Krouse, J. S. McMurray, S. Medina, K. O'Brien, D. R. Ouellette, B. J. Messinger-Rapport, R. J. Stachler, S. Strode, D. M. Thompson, J. C. Stemple, J. P. Willging, T. Cowley, S. McCoy, P. G. Bernad and M. M. Patel (2009). "Clinical practice guideline: Hoarseness (Dysphonia)." Otolaryngology-Head and Neck Surgery **141**(3): S1-S31. [PDF Full-Text](#)

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OBJECTIVE: This guideline provides evidence-based recommendations on managing hoarseness (dysphonia), defined as a disorder characterized by altered vocal quality, pitch, loudness, or vocal effort that impairs communication or reduces voice-related quality of life (QOL). Hoarseness affects nearly one-third of the population at some point in their lives. This guideline applies to all age groups evaluated in a setting where hoarseness would be identified or managed. It is intended for all clinicians who are likely to diagnose and manage patients with hoarseness. **PURPOSE:** The primary purpose of this guideline is to improve diagnostic accuracy for hoarseness (dysphonia), reduce inappropriate antibiotic use, reduce inappropriate steroid use, reduce inappropriate use of anti-reflux medications, reduce inappropriate use of radiographic imaging, and promote appropriate use of laryngoscopy, voice therapy, and surgery. In creating this guideline the American Academy of Otolaryngology-Head and Neck Surgery Foundation selected a panel representing the fields of neurology, speech-language pathology, professional voice teaching, family medicine, pulmonology, geriatric medicine, nursing, internal medicine, otolaryngology-head and neck surgery, pediatrics, and consumers. **RESULTS:** The panel made strong recommendations that 1) the clinician should not routinely prescribe antibiotics to treat hoarseness and 2) the clinician should advocate voice therapy for patients diagnosed with hoarseness that reduces voice-related QOL. The panel made recommendations that 1) the clinician should diagnose hoarseness (dysphonia) in a patient with altered voice quality, pitch, loudness, or vocal effort that impairs communication or reduces voice-related QOL; 2) the clinician should assess the patient with hoarseness by history and/or physical examination for factors that modify management, Such as one or more of the following: recent surgical procedures involving the neck or affecting the recurrent laryngeal nerve, recent endotracheal intubation. radiation treatment to the neck, a history of tobacco abuse, and occupation as a singer or vocal performer; 3) the clinician should Visualize the patient's larynx, or refer the patient to a clinician who can visualize the larynx, when hoarseness fails to resolve by a maximum of three months after onset, or irrespective of duration if a serious underlying cause is Suspected; 4) the clinician should not obtain Computed tomography or magnetic resonance imaging of the patient with a primary complaint of hoarseness prior to visualizing the larynx; 5) the clinician should not prescribe anti-reflux medications for patients with hoarseness without signs or symptoms of gastroesophageal reflux disease; 6) the clinician should not routinely prescribe oral corticosteroids to treat hoarseness; 7) the clinician should Visualize the larynx before prescribing voice therapy and document/communicate the results to the speech-language pathologists and 8) the clinician should prescribe, or refer the patient to a clinician who can prescribe, botulinum toxin injections for the treatment of hoarseness caused by adductor spasmodic dysphonia. The panel offered as options that 1) the clinician may perform laryngoscopy at any time in a patient with hoarseness, or may refer the patient to a clinician who can visualize the larynx; 2) the clinician may prescribe anti-reflux medication for patients with hoarseness and signs of chronic laryngitis; and 3) the clinician may educate/counsel patients with hoarseness about control/preventive measures. **DISCLAIMER:** This clinical practice guideline is not intended as a sole source of guidance in managing hoarseness (dysphonia). Rather, it is designed to assist clinicians by providing an evidence-based framework for decision-making strategies. The guideline is not intended to replace clinical judgment or establish a protocol for all individuals with this condition, and may not provide the only appropriate approach to diagnosing and managing this problem. (C) 2009 American Academy of Otolaryngology-Head and Neck Surgery Foundation. All rights reserved.

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Pathology

Barker, S. D., S. Bale, J. Booker, A. Buller, S. Das, K. Friedman, A. K. Godwin, W. W. Grody, E. Highsmith, J. A. Kant, E. Lyon, R. Mao, K. G. Monaghan, D. A. Payne, V. M. Pratt, I. Schrijver, A. E. Shrimpton, E. Spector, M. Telatar, L. Toji, K. Weck, B. Zehnbaauer and L. V. Kalman (2009). "Development and Characterization of Reference Materials for MTHFR, SERPINA1, RET, BRCA1, and BRCA2 Genetic Testing." [J Mol Diagn](#) **Epub Ahead of Print.** [PDF Full-Text](#)

From the Division of Laboratory Systems,* Centers for Disease Control and Prevention, Atlanta, Georgia; GeneDx, Inc., Gaithersburg, Maryland; Pathology and Laboratory Medicine, University of North Carolina, Chapel Hill; Molecular Genetics, Quest Diagnostics, San Juan Capistrano, California; Department of Genetics, University of Chicago, Chicago, Illinois; LabCorp, Burlington, North Carolina; Clinical Molecular Genetics Laboratory,** Fox Chase Cancer Center, Philadelphia, Pennsylvania; Divisions of Medical Genetics and Molecular Pathology, University of California, Los Angeles; Department of Laboratory Genetics, Mayo Clinic, Rochester, Minnesota; Department of Pathology and Human Genetics, University of Pittsburgh, Pittsburgh, Pennsylvania; Pathology Department and ARUP Laboratories, University of Utah, Salt Lake City; DNA Diagnostic Laboratory, Henry Ford Hospital, Detroit, Michigan; Department of Pathology,*** Southwestern Medical Center, Dallas, Texas; Quest Diagnostics, Nichols Institute, Chantilly, Virginia; Pathology Department, Stanford University School of Medicine, Stanford, California; Department of Clinical Pathology, SUNY Upstate Medical University, Syracuse, New York; Division of Medical Genetics, Department of Pediatrics, University of Colorado School of Medicine, Aurora; Molecular Genetics, Specialty Laboratories, Valencia, California; Coriell Institute for Medical Research,**** Camden, New Jersey; and Departments of Pathology, Immunology and Pediatrics, Washington University School of Medicine, St. Louis, Missouri.

Well-characterized reference materials (RMs) are integral in maintaining clinical laboratory quality assurance for genetic testing. These RMs can be used for quality control, monitoring of test performance, test validation, and proficiency testing of DNA-based genetic tests. To address the need for such materials, the Centers for Disease Control and Prevention established the Genetic Testing Reference Material Coordination Program (GeT-RM), which works with the genetics community to improve public availability of characterized RMs for genetic testing. To date, the GeT-RM program has coordinated the characterization of publicly available genomic DNA RMs for a number of disorders, including cystic fibrosis, Huntington disease, fragile X, and several genetic conditions with relatively high prevalence in the Ashkenazi Jewish population. Genotypic information about a number of other cell lines has been collected and is also available. The present study includes the development and commutability/genotype characterization of 10 DNA samples for clinically relevant mutations or sequence variants in the following genes: MTHFR; SERPINA1; RET; BRCA1; and BRCA2. DNA samples were analyzed by 19 clinical genetic laboratories using a variety of assays and technology platforms. Concordance was 100% for all samples, with no differences observed between laboratories using different methods. All DNA samples are available from Coriell Cell Repositories and characterization information can be found on the GeT-RM website.

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Pathology

Lee, H., A. M. Carlin, A. H. Ormsby and M. W. Lee (2009). "Brown bowel syndrome secondary to jejunioileal bypass: the first case report." *Obes Surg* **19**(8): 1176-9. [PDF Full-Text](#)

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

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Pulmonary & Critical Care Medicine

Khalid, I., Z. Q. Morris and B. DiGiovine (2009). "Specific Conductance Criteria for a Positive Methacholine Challenge Test: Are the American Thoracic Society Guidelines Rather Generous?" *Respiratory Care* **54**(9): 1168-1174. [Article Request Form](#)

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BACKGROUND: American Thoracic Society (ATS) guidelines for methacholine challenge testing (MCT) discuss specific airways conductance (sG_{aw}) as a surrogate marker for forced expiratory volume in the first second (FEV₁) to diagnose airways obstruction. The guidelines suggest a cutoff value of 45% drop in sG_{aw} to diagnose a positive MCT. However, there is no available evidence that supports this cutoff value of 45%. We conducted this study to examine the relationship between FEV₁ and sG_{aw} during MCT. **METHODS:** One-hundred thirty-eight patients who had both sG_{aw} and FEV₁ measured during MCT between April 2003 and March 2004 were retrospectively evaluated. The tests were done according to the ATS guidelines. Data were first analyzed using linear regression modeling, comparing the change in FEV₁ to changes in sG_{aw}. Then the sensitivity and specificity were generated for different cut points, using receiver operating characteristic analysis. **RESULTS:** Thirty-eight patients had a positive MCT based on ATS FEV₁ criteria. A decrease of 20% in FEV₁ correlated with a drop of 56% in sG_{aw} (95% confidence interval 52% to 60%, $r(2) = 0.35$, $P < .001$). Using 20% decline from baseline in FEV₁ at different PC₂₀ (provocational concentration that produced a $\geq 20\%$ FEV₁ decrease) values (4 mg/mL, 8 mg/mL, and 16 mg/mL), we then analyzed the sensitivity, specificity, positive predictive value, and negative predictive value of the 45% decline in sG_{aw} and compared it with a 56% decline in sG_{aw}. Using receiver operating characteristic analysis, we were able to find that a cutoff of 51-52% performed better than either of the 2 values. **CONCLUSIONS:** Our study suggests that the ATS suggested cutoff value of 45% decline in sG_{aw} to diagnose a positive MCT may be rather generous, and a decline of 51% from baseline may provide a more accurate measure of airway hyper-responsiveness. Further studies using well defined subjects with and without asthma should be done to better assess the test characteristics of sG_{aw}.

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Pulmonary & Critical Care Medicine

Swiderek, J., S. Morcos, V. Donthireddy, R. Surapaneni, V. Jackson-Thompson, L. Schultz, S. Kini and P. Kvale (2009). "Prospective Study to Determine the Volume of Pleural Fluid Required to Diagnose Malignancy." Chest **EPub Ahead of Print**. [Article Request Form](#)

Henry Ford Hospital.

BACKGROUND: The optimal volume of pleural fluid to diagnose a malignant effusion is unknown. Our study was designed to demonstrate if a minimum pleural fluid volume (10 mL) is equivalent to a large volume thoracentesis to make a cytopathological diagnosis of malignancy. **METHODS:** 121 thoracentesis samples were obtained from 102 patients with suspected or known malignant effusions. Pleural fluid was collected in three aliquots for cytological examination (10mL, 60mL, ≥ 150 mL). The pathologist was blinded to patient identifiers and aliquot volume. Sensitivity, specificity, negative predictive value (NPV), and positive predictive value (PPV) were calculated for each volume for the diagnosis of malignancy. **RESULTS:** Pleural malignancy was diagnosed in 90 patient encounters (74.4%). For direct smear/cytospin, there was increased sensitivity and NPV for 60 mL ($p = 0.0058$ and $p = 0.045$, respectively) and for ≥ 150 mL ($p < 0.001$ and $p = 0.009$, respectively) compared to 10 mL. For combined direct smear/cytospin and cell block preparations, statistical significance for sensitivity and NPV existed only between the 10 mL and ≥ 150 mL specimens ($p = 0.0099$ and $p = 0.033$, respectively). No statistical difference existed for specificity or PPV for any aliquot volume. **CONCLUSIONS:** The sensitivity for diagnosis of pleural malignancy is dependent on the pleural fluid volume extracted during thoracentesis. 10 mL volumes do not perform as well as larger volumes. When both direct smear/cytospin and cell block preparations are used, we recommend ≥ 150 mL, whereas when only direct smear/cytospin is used, 60 mL is adequate for the diagnosis a malignant pleural effusion.

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Radiation Oncology

Feigenberg, S. J., N. Sharma, J. Q. Yu, M. Buyyounouski, H. Borghaei, W. Scott, G. Simon, M. Unger and B. Movsas (2009). "Final report of a phase I Dose Escalation Trial of Stereotactic Body Radiotherapy (SBRT) for lung tumors." Journal of Thoracic Oncology **4(9)**: S943-S943. [Article Request Form](#)

[Feigenberg, Steven Joel; Sharma, Navesh; Yu, Jian Q.; Buyyounouski, Mark; Borghaei, Hossein; Scott, Walter; Simon, George; Unger, Michael] Fox Chase Canc Ctr, Philadelphia, PA 19111 USA. [Movsas, Benjamin] Henry Ford UNiv Hosp, Detroit, MI USA.

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Radiation Oncology

Feigenberg, S. J., N. Sharma, J. Q. Yu, B. Lally, H. Borghaei, R. Mehra, G. Simon, W. Scott, M. Buyyounouski, M. Unger and B. Movsas (2009). "Optimal PET response following stereotactic body radiotherapy (SBRT) for non-small cell lung cancer (NSCLC) is closely related to the pre-SBRT maximum standard uptake value." Journal of Thoracic Oncology 4(9): S734-S734. [Article Request Form](#)

[Feigenberg, Steven Joel; Sharma, Navesh; Yu Jian Q; Lally, Brian; Borghaei, Hossein; Mehra, Raneer; Simon, George; Scott, Walter; Buyyounouski, Mark; Unger, Michael] Fox Chase Canc Ctr, Philadelphia, PA 19111 USA. [Movsas, Benjamin] Henry Ford Univ Hosp, Detroit, MI USA.

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Radiation Oncology

Gore, E. M., K. Bae, C. Langer, M. Extermann, B. Movsas, P. Okunieff, G. Videtic and H. Choy (2009). "Phase I/II trial of a COX-2 inhibitor with limited field radiation for intermediate prognosis patients with locally advanced non-small cell lung cancer: Radiation Therapy Oncology Group (RTOG) 0213." Journal of Thoracic Oncology 4(9): S853-S854. [Article Request Form](#)

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Radiation Oncology

Haley, M., A. Konski, T. Li, J. D. Cheng, A. Maurer, O. Haluszka, W. Scott, N. J. Meropol, S. J. Cohen and G. Freedman (2009). "Influence of Diabetes on the Interpretation of PET Scans in Patients With Esophageal Cancer." Gastrointest Cancer Res 3(4): 149-52. PMC2739639. [PDF Full-Text](#)

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PURPOSE: Patients with diabetes mellitus (DM) can have altered sugar transport into cells, potentially affecting the results of 18-FDG PET scans. The specific aim of this study was to determine the effect of DM on pre- and post-treatment standard uptake value (SUV) scores in patients undergoing chemoradiotherapy for esophageal cancer. **METHODS:** Patients with locally advanced esophageal carcinoma undergoing preoperative or definitive chemoradiotherapy underwent pre- and posttreatment 18-FDG PET scans. Maximum SUV score was measured from the tumor before chemoradiotherapy and 3 to 4 weeks after chemoradiotherapy (preoperatively). Patients were identified as having DM by medical record review. Random serum glucose measurements were obtained prior to 18-FDG PET scans. The Wilcoxon signed-rank test was used to test for differences in SUV scores between patients with and without DM, and a generalized linear model with backward selection was applied to search for significant predictors of initial and posttreatment SUV scores. **RESULTS:** Sixty-three patients underwent 18-FDG PET scans during the course of treatment for esophageal malignancies between 6/02 and 8/05. Fifty-four patients received chemotherapy. The median radiation dose was 46.8 Gy. Eighteen patients had DM, six were insulin-dependent DM (IDDM). There was no difference in initial SUV scores between DM and non-DM patients ($P > .05$). There was also no difference in initial SUV scores between IDDM and non-IDDM groups. Patients with tumors at the gastroesophageal

junction had lower initial SUV scores compared to patients with tumors in the lower or mid-esophagus ($P = .05$). T stage was associated with initial SUV score (T2 lower than T3, $P = .014$). Older age ($P = .03$), diabetes ($P = .007$), higher T stage ($P = .002$), and presence of nodes ($P = .05$) were each positively associated with posttreatment SUV scores. Blood glucose levels prior to 18-FDG PET scan, endoscopic tumor length, and tumor location were not predictive of posttreatment SUV scores. Patients with DM had significantly lower posttreatment SUV scores compared to patients without DM ($P = .04$). Pathologic complete response or percent SUV decrease did not differ between patients with or without DM. **CONCLUSION:** Regardless of glucose levels, DM and IDDM do not influence pretreatment SUV scores in patients with localized esophageal cancer. However, DM may influence posttreatment SUV scores and thus complicate interpretation of treatment response. Further confirmatory study in a larger cohort of DM patients to evaluate the relationship of posttreatment SUV score to pathologic response is warranted.

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Radiation Oncology

Langer, C. J., B. Movsas, H. J. Ross, L. H. Wang, R. Jotte, S. Feigenberg, F. Xu, C. Huang, M. J. Monberg and C. K. Obasaju (2009). "Phase II trial of cisplatin (C), etoposide (E), and radiation (RT) followed by gemcitabine (G) vs G and docetaxel (D) in stage III A/B unresectable non-small cell lung cancer (NSCLC)." Journal of Thoracic Oncology 4(9): S518-S519. [Article Request Form](#)

[Langer, Corey J.] Univ Penn, Philadelphia, PA 19104 USA. [Movsas, Benjamin] Henry Ford Hlth Syst, Detroit, MI USA. [Wang Luhua] Canc Hosp & Inst CAMS & PUMC, Beijing, Peoples R China. [Ross, Helen J.] Mayo Clin, Scottsdale, AZ USA. [Jotte, Robert] Rocky Mt Canc Ctr, Denver, CO USA. US Oncol, Houston, TX USA. [Feigenberg, Steve] Fox Chase Canc Ctr, Philadelphia, PA 19111 USA. [Xu Feng] Sichuan Univ, W China Hosp, Chengdu 610064, Peoples R China. [Huang Chao] Kansas City VA Med Ctr, Kansas City, MO USA. [Monberg, Matthew J.; Obasaju, Coleman K.] Lilly USA, Indianapolis, IN USA.

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Radiation Oncology

Siddiqui, F., D. R. Ibrahim, I. Aref, M. Lu, W. S. Kim, D. Schultz and M. A. Elshaikh (2009). "Clinical outcome of pathologic Stage IIA endometrial adenocarcinoma after intravaginal brachytherapy alone." Brachytherapy 8(4): 396-400. [Article Request Form](#)

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

PURPOSE: We studied the impact of different prognostic factors on the clinical outcome for the patients with pathologic Stage IIA endometrial adenocarcinoma who had surgical staging (SS) and received adjuvant high-dose-rate intravaginal brachytherapy (IVB) alone. **METHODS AND MATERIALS:** Sixty-one patients with Stage IIA endometrial adenocarcinoma were retrospectively studied. Cox proportional hazards regression was used to study prognostic factors. **RESULTS:** All the patients underwent SS between July 1994 and December 2005. The median age was 64 years (range, 46-71 years). The median number of lymph nodes sampled was 8 (range, 7-12). All the patients received adjuvant IVB to doses of 35-36Gy in four to five fractions prescribed to the surface. The myometrial invasion was $<50\%$ in 33 patients and $\geq 50\%$ for 28 patients. The lymphovascular invasion (LVI) and the lower uterine segment involvement were identified in 18% and 61%, respectively. At a median followup of 64 months (range, 8-153 months), there were 7 patients who developed recurrences. On univariate analysis, the only factor significantly predictive for locoregional recurrence was LVI ($p=0.01$). In regard to overall survival (OS), factors that were significantly predictive on univariate analysis were LVI ($p=0.03$), tumor grade ($p=0.04$), and depth of myometrial invasion ($p=0.04$). The 5-year rates of vaginal and pelvic recurrences were 1.7% and 8.2%, respectively. The 5-year local control and OS rates were both 87%. **CONCLUSIONS:** Our results suggest excellent local control with adjuvant IVB alone for selected patients with Stage IIA endometrial adenocarcinoma. The patients with positive LVI and deep myometrial invasion have a worse locoregional control and OS despite SS and adjuvant IVB.

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Radiation Oncology

Siddiqui, F., C. J. Langer, K. Bae, J. Coyne, V. Gamerman, C. Bryan, R. Komaki, H. Choy, W. J. Curran, D. Watkins-Bruner and B. Movsas (2009). "Gender differences in survival

among lung cancer patients treated in radiation therapy oncology group (RTOG) trials." Journal of Thoracic Oncology 4(9): S524-S524. [Article Request Form](#)

[Siddiqui, Farzan; Movsas, Benjamin] Henry Ford Hlth Syst, Dept Radiat Oncol, Detroit, MI USA. [Langer, Corey J.; Coyne, James; Gamerman, Victoria; Bryan, Charlene; Watkins-Bruner, Deborah] Univ Penn, Philadelphia, PA 19104 USA. [Bae, Kyoung-hwa] RTOG, Dept Stat, Philadelphia, PA USA. [Komaki, Ritsuko] Univ Texas Houston, MD Anderson Canc Ctr, Houston, TX 77030 USA. [Choy, Hak] Univ Texas SW Med Ctr Dallas, Dallas, TX 75390 USA. [Curran, Walter J.] Emory Univ, Atlanta, GA 30322 USA.

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Radiation Oncology

Zhong, H. and J. V. Siebers (2009). "Monte Carlo dose mapping on deforming anatomy." Phys Med Biol 54(19): 5815-30. [Article Request Form](#)

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

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Sleep Medicine

Roth, T. (2009). "Sleep and society." Sleep Medicine 10: S1-S2. [PDF Full-Text](#)

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Sleep Medicine

Roth, T. (2009). "The Art of Good Sleep Proceedings of the 6th International Sleep Disorders Forum: Sleep and Society Conclusion." Sleep Medicine 10: S26-S26. [PDF Full-Text](#)

[Roth, Thomas] Henry Ford Hlth Syst, Sleep Disorders & Res Ctr, Detroit, MI 48202 USA. [Roth, Thomas] Wayne State Univ, Coll Med, Dept Psychiat, Detroit, MI USA.
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Surgery

Borgi, J., I. Rubinfeld, J. H. Patton, J. Ritz, J. Jordan and V. Velanovich (2009). "The association of morbidity mix and mortality in National Surgical Quality Improvement Program data." Journal of the American College of Surgeons 209(3): S97-S97. [PDF Full-Text](#)

[Borgi, Jamil; Rubinfeld, Ilan; Patton, Joe H.; Ritz, Jennifer; Jordan, Jack; Velanovich, Vic] Henry Ford Hosp, Detroit, MI 48202 USA.

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Surgery

Hoban, A. and V. Velanovich (2009). "Preoperative frailty and quality of life as predictors of postoperative complications." Journal of the American College of Surgeons **209**(3): S96-S96. [PDF Full-Text](#)

[Hoban, Adrienne; Velanovich, Vic] Henry Ford Hosp, Detroit, MI 48202 USA.

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Surgery

Lynch, R. J., A. K. Mathur, J. C. Hundley, J. Kubus, R. E. Pietroski, B. J. Mattice, J. D. Punch and M. J. Englesbe (2009). "Improving Organ Procurement Practices in Michigan." American Journal of Transplantation **9**(10): 2416-2423. [PDF Full-Text](#)

[Lynch, R. J.; Mathur, A. K.; Kubus, J.; Punch, J. D.; Englesbe, M. J.] Univ Michigan, Dept Surg, Div Transplantat, Ann Arbor, MI 48109 USA. [Hundley, J. C.] Henry Ford Hosp, Dept Surg, Transplant Inst, Detroit, MI 48202 USA. [Pietroski, R. E.; Mattice, B. J.] Gift Life Michigan, Ann Arbor, MI USA. Englesbe, MJ, Univ Michigan, Dept Surg, Div Transplantat, Ann Arbor, MI 48109 USA. englesbe@umich.edu

Travel to procure deceased donor organs is associated with risk to transplant personnel. In many instances, multiple teams are present for a given operation. We studied our statewide experience to determine how much excess travel this redundancy entails, and generated alternate models for organ recovery. We reviewed our organ procurement organization's experience with deceased donor operations between 2002 and 2008. Travel was expressed as cumulative person-miles between procurement team origin and donor hospital. A model of minimal travel was created, using thoracic and abdominal teams from the closest in-state center. A second model involved transporting donors to a dedicated procurement facility. Travel distance was recalculated using these models, and mode and cost of travel extrapolated from current practices. In 654 thoracic and 1469 abdominal donors studied, the mean travel for thoracic teams was 1066 person-miles and for abdominal teams was 550 person-miles. The mean distance traveled by thoracic and abdominal organs was 223 miles and 142 miles, respectively. Both hypothetical models showed reductions in team travel and reliance on air transport, with favorable costs and organ transport times compared to historical data. In summary, we found significant inefficiency in current practice, which may be alleviated using new paradigms for donor procurement.

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Urology

Diaz, M. (2009). "Editorial Comment." J Urol **Epub Ahead of Print**. [PDF Full-Text](#)

Vattikuti Urology Institute, Henry Ford Hospital, Detroit, Michigan.

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Urology

Patel, M. N., D. Eun, M. Menon and C. G. Rogers (2009). "Combined robotic-assisted laparoscopic partial nephrectomy and radical prostatectomy." JSLs **13**(2): 229-32. [Article Request Form](#)

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

A 59-year-old man with a history of prostate cancer and clear-cell renal-cell carcinoma of the kidney underwent a combined robot-assisted laparoscopic partial nephrectomy and radical prostatectomy. We describe the initial report of a combined robot-assisted operation for both procedures concurrently with a port strategy allowing reuse of ports.

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Urology

Sivanandam, A., S. Siva and M. Bhandari (2009). "Re: Repair of Giant Vesicovaginal Fistulas." Journal of Urology **182**(4): 1655-1655. [PDF Full-Text](#)

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