

Henry Ford Health System Publication List - April 2010

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Allergy & Immunology

Sikka, N., G. Wegienka, S. Havstad, J. Genaw, A. M. Carlin and E. Zoratti (2010). "Respiratory medication prescriptions before and after bariatric surgery." Ann Allergy Asthma Immunol **104**(4): 326-30. [Article Request Form](#)

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BACKGROUND: Increased body mass index is associated with asthma and frequent respiratory complaints. Bariatric surgery often results in rapid weight loss associated with an improved respiratory status. **OBJECTIVE:** To assess whether patients undergoing bariatric surgery would have fewer respiratory symptoms after surgery as evidenced by decreases in respiratory prescription drug claims. **METHODS:** A retrospective cohort of 320 patients continuously enrolled in a large, southeast Michigan health maintenance organization were studied for 1 year before and 1 year after bariatric surgery. The health maintenance organization claims database was used to compare respiratory prescriptions filled before and after surgery. Respiratory medications included bronchodilator inhalers, inhaled corticosteroids, oral corticosteroids, theophylline, and leukotriene antagonists. **RESULTS:** Of 320 surgical patients, 64 (20%) filled at least 1 respiratory medication prescription for a total of 468 prescriptions during the 2-year observation period. Of the prescriptions filled, 35% were beta-agonists, 38% inhaled corticosteroids, 12% oral corticosteroids, 15% leukotriene antagonists, and less than 1% theophylline. Total respiratory medication prescription fills decreased by 49% (from 314 to 154 prescriptions) in the postsurgical year, with only 43.1% of patients filling prescriptions in the year before surgery also filling a prescription in the postsurgical surveillance period. Analyses restricted to 40 patients with physician-diagnosed asthma revealed mean (SD) presurgical prescription fills of 7.0 (6.9) per year, decreasing to 3.8 (6.1) per year in the postsurgical year ($P = .002$). **CONCLUSION:** Respiratory medication use decreases significantly after bariatric surgery. A secondary benefit of bariatric surgery may include a decrease in respiratory symptoms and concomitant medication use.

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Anesthesiology

Frogel, J. and D. Galusca (2010). "Anesthetic considerations for patients with advanced valvular heart disease undergoing noncardiac surgery." Anesthesiol Clin **28**(1): 67-85. [PDF Full-Text](#)

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Patients with valvular heart disease represent a growing segment of the population and can present major challenges to clinical anesthesiologists. This review focuses on patients with advanced left-sided valvular disease undergoing noncardiac surgery. The pathophysiology and anesthetic implications of aortic stenosis and insufficiency and mitral stenosis and insufficiency are discussed, with a focus on optimizing perioperative management and decision making for patients with these conditions.

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Biostatistics & Research Epidemiology

Harel, Z., C. C. Johnson, M. A. Gold, B. Cromer, E. Peterson, R. Burkman, M. Stager, R. Brown, A. Bruner, S. Coupey, P. Hertweck, H. Bone, K. Wolter, A. Nelson, S. Marshall and L. K. Bachrach (2010). "Recovery of bone mineral density in adolescents following the use of depot medroxyprogesterone acetate contraceptive injections." Contraception **81**(4): 281-291. [Article Request Form](#)

[Harel, Zeev] Brown Univ, Div Adolescent Med, Hasbro Childrens Hosp, Providence, RI 02903 USA. [Harel, Zeev] Brown Univ, Dept Pediat, Warren Alpert Med Sch, Providence, RI 02903 USA. [Johnson, Christine Cole; Peterson, Edward] Henry Ford Hlth Syst, Dept Biostat & Res Epidemiol, Detroit, MI 48202 USA. [Gold, Melanie A.] Univ Pittsburgh, Student Hlth Serv, Div Student Affairs, Pittsburgh, PA 15213 USA. [Gold, Melanie A.] Univ Pittsburgh, Div Adolescent Med, Dept Pediat, Pittsburgh, PA 15213 USA. [Cromer, Barbara; Stager, Margaret] Case Western Reserve Univ, Sch Med, Div Adolescent Med, MetroHlth Med Ctr, Cleveland, OH 44109 USA. [Cromer, Barbara; Stager, Margaret] Case Western Reserve Univ, Sch Med, Dept Pediat, Cleveland, OH 44109 USA. [Burkman, Ronald] Baystate Med Ctr, Dept Obstet & Gynecol, Div Gen Obstet & Gynecol, Springfield, MA 01199 USA. [Brown, Robert] Ohio State Univ, Coll Med, Dept Pediat, Columbus, OH 43210 USA. [Bruner, Ann] Johns Hopkins Univ, Sch Med, Dept Pediat, Div Gen Pediat & Adolescent Med, Baltimore, MD 21287 USA. [Coupey, Susan] Albert Einstein Coll Med, New York, NY 10467 USA. [Coupey, Susan] Childrens Hosp Montefiore, Div Adolescent Med, New York, NY 10467 USA. [Hertweck, Paige] Univ Louisville, Dept Obstet Gynecol & Women Hlth, Sch Med, Louisville, KY 40202 USA. [Bone, Henry] Michigan Bone & Mineral Clin, Detroit, MI 48236 USA. [Wolter, Kevin] Pfizer Global Res & Dev, New London, CT 06320 USA. [Nelson, Anita] Harbor UCLA Med Ctr, Dept Obstet & Gynecol, Torrance, CA 90509 USA. [Marshall, Sharon] Childrens Hosp Michigan, Div Adolescent Med, Detroit, MI 48201 USA. [Marshall, Sharon] Wayne State Univ, Sch Med, Detroit, MI 48201 USA. [Bachrach, Laura K.] Stanford Univ, Sch Med, Div Pediat Endocrinol, Stanford, CA 94305 USA.

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Background: Depot medroxyprogesterone acetate (DMPA) is a highly effective progestin-only contraceptive that is widely used by adolescents. We investigated bone mineral density (BMD) changes in female adolescents during and following use of this method. Study Design: A multicenter, prospective, non-randomized observational study in 98 healthy female adolescents aged 12-18 years who initiated DMPA intramuscular injections for contraception and provided BMD data for up to 240 weeks while receiving DMPA and for up to 300 weeks after DMPA cessation. BMD at the lumbar spine (LS), total hip (TH) and femoral neck (FN) was assessed by dual-energy X-ray absorptiometry. A mixed model analysis of variance was used to examine BMD changes. Results: At the time of their final DMPA injection, participants had mean BMD declines from baseline of 2.7% (LS), 4.1% (TH) and 3.9% (FN) ($p < .001$ at all three sites). Within 60 weeks of discontinuation of DMPA, mean LS BMD had returned to baseline levels, and 240 weeks after DMPA discontinuation, the mean LS BMD was 4.7% above baseline. Mean TH and FN BMD values recovered to baseline values more slowly: 240 weeks and 180 weeks, respectively, after the last DMPA injection. Conclusions: BMD loss in female adolescents receiving DMPA for contraception is substantially or fully reversible in most girls following discontinuation of DMPA, with faster recovery at the LS than at the hip. (C) 2010 Elsevier Inc. All rights reserved.

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Biostatistics & Research Epidemiology

Miller, L., L. D. Lemke, X. H. Xu, S. M. Molaroni, H. Y. You, A. J. Wheeler, J. Booza, A. Grgicak-Mannion, R. Krajenta, P. Graniero, H. Krouse, L. Lamerato, D. Raymond, J. Reiners and L. Weglicki (2010). "Intra-urban correlation and spatial variability of air toxics across an international airshed in Detroit, Michigan (USA) and Windsor, Ontario (Canada)." Atmospheric Environment **44**(9): 1162-1174. [Article Request Form](#)

[Miller, Lindsay; Xu, Xiaohong] Univ Windsor, Dept Civil & Environm Engrn, Windsor, ON N9B 3P4, Canada. [Lemke, Lawrence D.; Molaroni, Shannon M.] Wayne State Univ, Dept Geol, Detroit, MI USA. [You, Hongyu; Wheeler, Amanda J.] Hlth Canada, Air Hlth Sci Div, Ottawa, ON K1A 0L2, Canada. [Booza, Jason] Wayne State Univ, Dept Family Med, Detroit, MI USA. [Grgicak-Mannion, Alice; Graniero, Phillip] Univ Windsor, Great Lakes Inst Environm Res, Windsor, ON N9B 3P4, Canada. [Krajenta, Richard; Lamerato, Lois] Henry Ford Hlth Syst, Detroit, MI USA. [Krouse, Helene; Weglicki, Linda] Wayne State Univ, Coll Nursing, Detroit, MI 48202 USA. [Raymond, Delbert] Eastern Michigan Univ, Sch Nursing, Ypsilanti, MI 48197 USA. [Reiners, John, Jr.] Wayne State Univ, Inst Environm Hlth Sci, Detroit, MI USA. Lemke, LD, 0224 Old Main, 4841 Cass, Detroit, MI 48202 USA. ldlemke@wayne.edu

As part of a larger research project initiated by the Geospatial Determinants of Health Outcomes Consortium (GeoDHOC), an air quality study was conducted in an international airshed encompassing Detroit, Michigan, USA, and Windsor, Ontario, Canada. Active and passive samplers were used to measure nitrogen dioxide (NO₂), sulfur dioxide (SO₂), 26 volatile organic compounds (VOCs), 23 polycyclic aromatic hydrocarbons (PAHs) and pesticides, and three size fractions of particulate matter (PM) over a two-week period in September, 2008. Measurements of NO₂ and 14 VOCs were found to be acceptable at 98 out of 100 passive monitoring sites. PAH and PM measurements were acceptable at 38 out of 50 active sites. Mean concentrations for all analytes except for PM_{2.5-10} were higher in Detroit than Windsor by a factor of up to 1.8. Strong statistical correlations were found among benzene, toluene, ethylbenzene, and xylene (BTEX), as well as between NO₂ and PM in Detroit. In Windsor, the strongest correlations were between NO₂ and total VOCs, as well as total PAHs and total VOCs. Differences in the degree of correlation observed in Detroit and Windsor are attributable to differences in the volume and composition of emissions within the two cities. Spatial variability was evaluated using a combination of statistical (coefficient of variation) and geostatistical (standardized variogram slope) metrics together with concentration maps. Greater spatial variability was observed for total VOCs and total BTEX in Detroit, while greater variability of NO₂, total PAHs, and PM was found in Windsor. Results of this study suggest that statistical correlations between NO₂ and other contaminants may not provide sufficient justification for the indiscriminant use of NO₂ as a proxy for those contaminants if smaller scale features are to be reproduced. (C) 2009 Elsevier Ltd. All rights reserved.

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Bone & Joint Center

Holcomb, J. O., D. J. Hebert, M. A. Mighell, P. E. Dunning, D. R. Pupello, M. D. Pliner and M. A. Frankle (2010). "Reverse shoulder arthroplasty in patients with rheumatoid arthritis." J Shoulder Elbow Surg **EPub Ahead of Print**. [PDF Full-Text](#)

Henry Ford Wyandotte Hospital, Wyandotte, MI.

BACKGROUND: The purpose of this study was to describe the pathoanatomy of patients diagnosed with rheumatoid arthritis and rotator cuff deficiency and report their outcomes following reverse shoulder arthroplasty. **METHODS:** Twenty-one shoulders were evaluated prospectively. Nine had no prior surgery, 9 had a failed rotator cuff repair, and 3 had a failed arthroplasty. Patients were followed for a minimum of 2 years (average, 36 months). All patients had preoperative radiographs and 19 shoulders had an MRI or CT available for evaluation of muscular and bony deficiency. Radiographs at most recent follow-up were evaluated for loosening and scapular notching. **RESULTS:** All outcome measures improved significantly: ASES scores improved from 28 preoperatively to 82 postoperatively ($P < .0001$); SST scores improved from 1 to 7 ($P < .0001$); VAS pain scores improved from 7 to 1 ($P < .0001$); VAS function scores improved from 3 to 6 ($P = .0058$); elevation improved from 52(degrees) to 126(degrees) ($P < .0001$); abduction improved from 55(degrees) to 116(degrees) ($P = .0002$); external rotation improved from 19(degrees) to 33(degrees) ($P = .02$); and internal rotation improved from S1 to L4 ($P = .02$). Twelve patients rated their outcome as excellent, 6 as good, 2 as satisfactory, and 1 as unsatisfactory. Severe glenoid erosion was seen in 10 of the shoulders and 5 of the defects required structural grafting. Three patients (14%) sustained a complication that required reoperation: 2 for infection and 1 for periprosthetic fracture. **CONCLUSIONS:** In patients with rheumatoid arthritis and rotator cuff deficiency, reverse shoulder arthroplasty can provide improvement in function and decreased pain. **LEVEL OF EVIDENCE:** Level IV, Case Series, Treatment Study.

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Bone & Joint Center

McDonald, C. P., C. C. Bachison, V. Chang, S. W. Bartol and M. J. Bey (2010). "Three-dimensional dynamic in vivo motion of the cervical spine: assessment of measurement accuracy and preliminary findings." Spine J **EPub Ahead of Print**. [Article Request Form](#)

Bone and Joint Center, Henry Ford Hospital, Detroit, MI 48202, USA.

BACKGROUND CONTEXT: Previous research has quantified cervical spine motion with conventional measurement techniques (eg, cadaveric studies, motion capture systems, and fluoroscopy), but these techniques were not designed to accurately measure three-dimensional (3D) dynamic cervical spine motion under in vivo conditions. **PURPOSE:** The purposes of this study were to characterize the accuracy of model-based tracking for measuring 3D dynamic cervical spine kinematics and to demonstrate its in vivo application. **STUDY DESIGN:** Through accuracy assessment and application of technique, in vivo cervical spine motion was measured. **METHODS:** The accuracy of model-based tracking for measuring cervical spine motion was determined in an in vitro experiment. Tantalum beads were implanted into the vertebrae of an ovine specimen, and biplane X-ray images were acquired as the specimen's neck was manually moved through neck extension and axial neck rotation. The 3D position and orientation of each cervical vertebra were determined from the biplane X-ray images using model-based tracking. For comparison, the position and orientation of each vertebra were also determined by tracking the position of the implanted beads with dynamic radiostereometric analysis. To demonstrate in vivo application of this technique, biplane X-ray images were acquired as a human subject performed two motion tasks: neck extension and axial neck rotation. The positions and orientations of each cervical vertebra were determined with model-based tracking. Cervical spine motion was reported with standard kinematic descriptions of translation and rotation. **RESULTS:** The in vitro validation demonstrated that model-based tracking is accurate to within +/-0.6 mm and +/-0.6 degrees for measuring cervical spine motion. For the in vivo application, there were significant rotations about all three anatomical axes for both the neck extension and axial neck rotation motion tasks. **CONCLUSIONS:** Model-based tracking is an accurate technique for measuring in vivo, 3D, dynamic cervical spine motion. Preliminary data acquired using this technique are in agreement with previous studies. It is anticipated that this experimental approach will enhance our understanding of cervical spine motion under normal and pathologic conditions.

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Bone & Joint Center

Scher, S., K. Anderson, N. Weber, J. Bajorek, K. Rand and M. J. Bey (2010). "Associations Among Hip and Shoulder Range of Motion and Shoulder Injury in Professional Baseball Players." Journal of Athletic Training **45**(2): 191-197. [PDF Full-Text](#)

[Scher, Steve] Team Rehabil, Royal Oak, MI 48073 USA. [Anderson, Kyle] William Beaumont Hosp, Royal Oak, MI 48072 USA. [Weber, Nick; Bajorek, Jeff] Henry Ford Hosp, Dept Orthopaed, Detroit, MI 48202 USA. [Rand, Kevin] Detroit Tigers Baseball Inc, Detroit, MI USA. [Bey, Michael J.] Henry Ford Hosp, Ctr Bone & Joint, Detroit, MI 48202 USA.

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Context: The overhead throwing motion is complex, and restrictions in range of motion (ROM) at the hip may place additional demands on the shoulder that lead to injury. However, the relationship between hip and shoulder ROM in athletes with and without a history of shoulder injury is unknown. **Objective:** To (1) determine if differences exist in hip and shoulder ROM between professional baseball players with a history of shoulder injury and those with no history of shoulder injury and (2) assess relationships between hip and shoulder ROM in these players. **Design:** Cross-sectional study. **Patients or Other Participants:** Fifty-seven professional baseball players. **Main Outcome Measure(s):** Outcome measures consisted of hip extension and internal rotation, shoulder internal and external rotation, glenohumeral internal-rotation deficit, and history of shoulder injury. Differences in shoulder and hip ROM were assessed with a 1-way analysis of variance. Associations between hip and shoulder ROM were assessed with linear regression. **Results:** Nonpitchers with a history of shoulder injury had more external rotation and less internal rotation of the shoulder than nonpitchers with no history of shoulder injury. Glenohumeral internal-rotation deficit was greater in both pitchers and nonpitchers with a history of shoulder injury. The relationship between dominant hip extension and shoulder external rotation was significant for pitchers with a history of shoulder injury and nonpitchers with a history of shoulder injury. **Conclusions:** Shoulder injury may be associated with specific measures of hip and shoulder ROM, and hip extension and shoulder external rotation may be related in baseball players with a history of shoulder injury. Additional research is necessary to understand the specific mechanisms of shoulder injury in the throwing athlete.

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Cardiology

Al-Mallah, M. H., A. Sitek, S. C. Moore, M. Di Carli and S. Dorbala (2010). "Assessment of myocardial perfusion and function with PET and PET/CT." J Nucl Cardiol **EPub Ahead of Print**. [PDF Full-Text](#)

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Cardiology

Hammoud, Z. T., Y. Mechref, A. Hussein, S. Bekesova, M. Zhang, K. A. Kesler and M. V. Novotny (2010). "Comparative glycomic profiling in esophageal adenocarcinoma." J Thorac Cardiovasc Surg **139**(5): 1216-23. [PDF Full-Text](#)

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OBJECTIVE: Aberrant glycosylation has been implicated in various types of cancers. Cancerous cells with altered glycosylation of their surface proteins shed such proteins into the circulating fluids. Glycomic profiling of such fluids shows the altered glycosylation. We performed glycomic profiling of serum from patients with no known disease, Barrett's without dysplasia, with high-grade dysplasia, and with esophageal adenocarcinoma in an attempt to delineate distinct differences in glycosylation among these groups. METHODS: Serum samples from patients with Barrett's metaplasia (N = 5), high-grade dysplasia (N = 11), and esophageal adenocarcinoma (N = 50) were collected; samples from 18 healthy volunteers were used as control. Serum N-glycans were enzymatically released and then applied to both C18 Sep-Pak (Waters, Milford, MA) cartridges and activated charcoal cartridges. N-glycans were permethylated and then spotted directly onto a matrix-assisted laser desorption ionization plate. Mass spectra were acquired using the Applied Biosystems 4800 MALDI TOF/TOF Analyzer (Applied Biosystems Inc, Framingham, Mass). The obtained matrix-assisted laser desorption ionization-mass spectrometry data were processed using DataExplorer files (Applied Biosystems Inc) listing m/z values and intensities. RESULTS: The intensities of 98 glycans were significantly different among the 3 groups; 26 of these corresponded to known glycan structures. Pairwise comparisons showed that 8 glycans were significantly different in all 3 pairwise comparisons. CONCLUSION: We demonstrated that comparative glycomic profiling of esophageal adenocarcinoma reveals a subset of glycans that can be selected as candidate biomarkers. These markers can differentiate normal from high-grade dysplasia, normal from esophageal adenocarcinoma, and high-grade dysplasia from esophageal adenocarcinoma. Further validation will be necessary to determine the clinical utility of these glycan biomarkers.

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Cardiology

Khawaja, O. and M. H. Al-Mallah (2010). "Safety of Concomitant Use of Proton Pump Inhibitors and Clopidogrel." American Journal of Medicine **123**(4): E11-E11. [PDF Full-Text](#)

[Khawaja, Owais] Providence Hosp, Dept Internal Med, Southfield, MI 48037 USA. [Khawaja, Owais; Al-Mallah, Mouaz H.] Wayne State Univ, Sch Med, Dept Internal Med, Detroit, MI 48201 USA. [Al-Mallah, Mouaz H.] Henry Ford Hlth Syst, Detroit, MI USA.

Khawaja, O, Providence Hosp, Dept Internal Med, Southfield, MI 48037 USA.

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Cardiology

Lanfeard, D. E. (2010). "Genetic variation in the natriuretic peptide system and heart failure." Heart Failure Reviews **15**(3): 219-228. [PDF Full-Text](#)

Henry Ford Hosp, Sect Adv Heart Failure & Cardiac Transplantat, Henry Ford Heart & Vasc Inst, Detroit, MI 48202 USA.

Lanfeard, DE, Henry Ford Hosp, Sect Adv Heart Failure & Cardiac Transplantat, Henry Ford Heart & Vasc Inst, 2799 W Grand Blvd,K14, Detroit, MI 48202 USA. dlanfea1@hfhs.org

Heart failure (HF) is a modern epidemic and is one of the few cardiovascular diseases which is increasing in prevalence. The growing importance of the Natriuretic Peptide (NP) system in HF is well recognized.

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

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Center for Health Promotion & Disease Prevention

Tammemagi, C. M., R. M. Davis, M. S. Benninger, A. L. Holm and R. Krajenta (2010). "Secondhand Smoke as a Potential Cause of Chronic Rhinosinusitis A Case-Control Study." *Archives of Surgery* **145**(4): 327-334. [Article Request Form](#)

[Tammemagi, C. Martin] Brock Univ, Dept Community Hlth Sci, St Catharines, ON L2S 3A1, Canada. [Davis, Ronald M.; Holm, Amanda L.; Krajenta, Richard] Henry Ford Hlth Syst, Detroit, MI USA. [Benninger, Michael S.] Cleveland Clin, Cleveland, OH 44106 USA.
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Objective: To assess the role of secondhand smoke (SHS) in the etiology of chronic rhinosinusitis (CRS).
Design: Matched case-control study. Associations between SHS and CRS were evaluated by conditional logistic regression odds ratios. **Setting:** Henry Ford Health System, Detroit, Michigan. **Participants:** A total of 306 nonsmoking patients diagnosed as having an incident case of CRS and 306 age-matched, sex-matched, and race/ethnicity-matched non-smoking control patients. **Main Outcome Measures:** Exposure to SHS for the 5 years before diagnosis of CRS (case patients) and before study entry (controls) for 4 primary sources: home, work, public places, and private social functions outside the home, such as parties, dinners, and weddings. **Results:** Of controls and case patients, respectively, 28 (9.1%) and 41 (13.4%) had SHS exposure at home, 21 (6.9%) and 57 (18.6%) at work, 258 (84.3%) and 276 (90.2%) in public places, and 85 (27.8%) and 157 (51.3%) at private social functions. Adjusted for potential confounders (socioeconomic status and exposures to air pollution and chemicals or respiratory irritants from hobbies, work, or elsewhere), the odds ratios for CRS were 1.69 (95% confidence interval, 0.92-3.10) for SHS exposure at home, 2.81 (1.42-5.57) for exposure at work, 1.48 (0.88-2.49) for exposure in public places, and 2.60 (1.74-3.89) for exposure at private functions. A strong, independent dose-response relationship existed between CRS and the number of venues where SHS exposure occurred (odds ratio per 1 of 4 levels, 2.03; 95% confidence interval, 1.55-2.66). Approximately 40.0% of CRS appeared to be attributable to SHS. **Conclusions:** Exposure to SHS is common and significantly independently associated with CRS. These findings have important clinical and public health implications.

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Dermatology

Gold, L. S. (2010). "Fixed-Combination Products in the Management of Acne Vulgaris." *Cutis* **85**(3): 160-167. [PDF Full-Text](#) (ID=sladenjournals.hfhs.org / PW=henry)

Henry Ford Hosp, Dept Dermatol, Henry Ford Med Ctr, Detroit, MI 48202 USA.
Gold, LS, Henry Ford Hosp, Dept Dermatol, Henry Ford Med Ctr, New Ctr 1,3031 W Grand Blvd,Ste 800, Detroit, MI 48202 USA. lstein1@hfhs.org

Acne vulgaris is the most common dermatologic disorder in the United States. Although its cause is unknown, various factors are implicated in its pathogenesis. No single topical antiacne medication acts on all the major pathophysiologic events. Combined use of agents with different modes of action provides better patient outcomes than monotherapy. Topical fixed-combination therapies include antibiotics with benzoyl peroxide (BPO) or retinoids, and retinoids with BPO. With increased efficacy can come increased irritation from the combination or formulation excipients. Surfactants, preservatives, and high levels of organic solvents including

alcohols found in some products are potential irritants. This review considers data on topical fixed-combination acne medications and developments focused on newer lower concentration, optimized formulations aimed at reducing dryness and irritation without compromising efficacy. In the absence of direct comparative clinical trials, this review provides timely guidance for clinicians on the use of these agents. *Cutis*. 2010;85:160-167.

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Dermatology

Mahmoud, B. H., E. Ruvolo, C. L. Hexsel, Y. Liu, M. R. Owen, N. Kollias, H. W. Lim and I. H. Hamzavi (2010). "Impact of Long-Wavelength UVA and Visible Light on Melanocompetent Skin." *J Invest Dermatol* **Epub Ahead of Print**. [PDF Full-Text](#)

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

The purpose of this study was to determine the effect of visible light on the immediate pigmentation and delayed tanning of melanocompetent skin; the results were compared with those induced by long-wavelength UVA (UVA1). Two electromagnetic radiation sources were used to irradiate the lower back of 20 volunteers with skin types IV-VI: UVA1 (340-400 nm) and visible light (400-700 nm). Pigmentation was assessed by visual examination, digital photography with a cross-polarized filter, and diffused reflectance spectroscopy at 7 time points over a 2-week period. Confocal microscopy and skin biopsies for histopathological examination using different stains were carried out. Irradiation was also carried out on skin type II. Results showed that although both UVA1 and visible light can induce pigmentation in skin types IV-VI, pigmentation induced by visible light was darker and more sustained. No pigmentation was observed in skin type II. The quality and quantity of pigment induced by visible light and UVA1 were different. These findings have potential implications on the management of photoaggravated pigmentary disorders, the proper use of sunscreens, and the treatment of depigmented lesions. *Journal of Investigative Dermatology* advance online publication, 22 April 2010; doi:10.1038/jid.2010.95.

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Dermatology

Mahmoud, B. H., D. Srivastava, J. J. Janiga, J. J. Yang, H. W. Lim and D. M. Ozog (2010). "Safety and Efficacy of Erbium-Doped Yttrium Aluminum Garnet Fractionated Laser for Treatment of Acne Scars in Type IV to VI Skin." *Dermatol Surg* **Epub Ahead of Print**. [PDF Full-Text](#)

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

BACKGROUND Ablative resurfacing lasers are effective for treatment of acne scars, but they have a high risk of complications. Fractional lasers have less severe side effects but more moderate efficacy than ablative devices. Studies were performed in individuals with Fitzpatrick skin type I to VI. **OBJECTIVE** To determine the efficacy and safety of an erbium 1,550-nm fractional laser in the treatment of facial acne scars in Fitzpatrick skin types IV to VI. **METHODS** We conducted a prospective, single-blind, randomized trial in patients with acne scars (n=15), skin type IV to VI, with a 1,550-nm erbium fractionated laser. Patients were divided into two groups; one was treated with 10 mJ and the other with 40 mJ. Five monthly laser sessions were performed. A patient questionnaire was distributed. **RESULTS** There was a significant improvement in the acne scarring and overall appearance (p<.001). No significant difference was found between 10 and 40 mJ. Patients were highly satisfied with their results. Significant postinflammatory hyperpigmentation was seen; pain was significantly higher in darker skin. **CONCLUSIONS** Fractional photothermolysis is effective for the treatment of acne scars, but practitioners should be aware of the higher incidence of pain and postinflammatory hyperpigmentation in individuals with skin types IV to VI. The study was funded by Reliant Technologies, Inc., which participated in the study design. Galderma (Ft. Worth, TX) provided Tri-luma cream and GlaxoSmithKline (Research Triangle Park, NC) provided valacyclovir (Valtrex).

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Diagnostic Radiology

Akhondi-Asl, A., K. Jafari-Khouzani, K. Elisevich and H. Soltanian-Zadeh (2010). "Hippocampal volumetry for lateralization of temporal lobe epilepsy: Automated versus manual methods." *Neuroimage* **Epub Ahead of Print**. [Article Request Form](#)

Control and Intelligent Processing Center of Excellence (CIPCE), School of Electrical and Computer Engineering, University of Tehran, Tehran, Iran; School of Cognitive Sciences, Institute for Studies in Theoretical Physics and Mathematics (IPM), Tehran, Iran; Department of Diagnostic Radiology, Henry Ford Hospital, Detroit, MI 48202, USA.

The hippocampus has been the primary region of interest in the preoperative imaging investigations of mesial temporal lobe epilepsy (mTLE). Hippocampal imaging and electroencephalographic features may be sufficient in several cases to declare the epileptogenic focus. In particular, hippocampal atrophy, as appreciated on T1-weighted (T1W) magnetic resonance (MR) images, may suggest a mesial temporal sclerosis. Qualitative visual assessment of hippocampal volume, however, is influenced by head position in the magnet and the amount of atrophy in different parts of the hippocampus. An entropy-based segmentation algorithm for subcortical brain structures (LocallInfo) was developed and supplemented by both a new multiple atlas strategy and a free-form deformation step to capture structural variability. Manually segmented T1-weighted magnetic resonance (MR) images of 10 non-epileptic subjects were used as atlases for the proposed automatic segmentation protocol which was applied to a cohort of 46 mTLE patients. The segmentation and lateralization accuracies of the proposed technique were compared with those of two other available programs, HAMMER and FreeSurfer, in addition to the manual method. The Dice coefficient for the proposed method was 11% ($p < 10^{-5}$) and 14% ($p < 10^{-4}$) higher in comparison with the HAMMER and FreeSurfer, respectively. Mean and Hausdorff distances in the proposed method were also 14% ($p < 0.2$) and 26% ($p < 10^{-3}$) lower in comparison with HAMMER and 8% ($p < 0.8$) and 48% ($p < 10^{-5}$) lower in comparison with FreeSurfer, respectively. LocallInfo proved to have higher concordance (87%) with the manual segmentation method than either HAMMER (85%) or FreeSurfer (83%). The accuracy of lateralization by volumetry in this study with LocallInfo was 74% compared to 78% with the manual segmentation method. LocallInfo yields a closer approximation to that of manual segmentation and may therefore prove to be more reliable than currently published automatic segmentation algorithms.

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Diagnostic Radiology

Jain, R. and M. Levine (2010). "Correction to the Relative Risk Calculation for Gadolinium-enhanced MR Imaging and Nephrogenic Systemic Fibrosis." *Radiology* **255**(1): 307-308.

[PDF Full-Text](#)

[Jain, Rajan] Henry Ford Hlth Syst, Dept Radiol, Div Neuroradiol, Detroit, MI 48202 USA. [Levine, Mitchell] McMaster Univ, Dept Clin Epidemiol & Biostat, Hamilton, ON, Canada.

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Diagnostic Radiology

Pineda, C., A. M. Reginato, V. Flores, M. Aliste, M. Alva, R. A. Aragon-Lainez, A. B. Gonzalez, J. A. Bouffard, C. V. Caballero-Urbe, M. Chavez-Lopez, N. N. Chavez-Perez, P. Collado, J. F. Diaz-Coto, M. Duarte, E. Filippucci, C. Galarza-Maldonado, A. Garcia-Kutzbach, F. J. Godoy, E. Gonzalez-Sevillano, I. G. Da Silveira, M. Gutierrez, C. Hernandez-Diaz, J. Hernandez, M. Lamuno-Encorrada, J. C. Marcos, N. Marin-Arriaga, J. A. Mendonca, J. Michaud, C. Moya, R. Munoz-Louis, F. Neubarth, M. Quintero, B. Reyes, S. Ruta, P. J. Rodriguez-Henriquez, C. Solano, L. Ventura-Rios, I. Moller and E. Naredo (2010). "Pan-American League of Associations for Rheumatology (PANLAR)

Recommendations and Guidelines for Musculoskeletal Ultrasound Training in the Americas for Rheumatologists." *Jcr-Journal of Clinical Rheumatology* **16**(3): 113-118. [PDF Full-Text](#)

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Objective: To develop guidelines for Musculoskeletal Ultrasound (MSKUS) training for rheumatologists in the Americas. Methods: A total of 25 Rheumatologists from 19 countries of the American Continent participated in a consensus-based interactive process (Delphi method) using 2 consecutive electronic questionnaires. The first questionnaire included the following: the relevance of organizing courses to teach MSKUS to Rheumatologists, the determination of the most effective educational course models, the trainee levels, the educational objectives, the requirements for passing the course(s), the course venues, the number of course participants per instructor, and the percentage of time spent in hands-on sessions. The second questionnaire consisted of questions that did not achieve consensus (>65%) in the first questionnaire, topics, and pathologies to be covered at each course MSKUS level. Results: General consensus was obtained for MSKUS courses to be divided into 3 educational levels: basic, intermediate, and advanced. These courses should be taught using a theoretical-didactic and hands-on model. In addition, the group established the minimum requirements for attending and passing each MSKUS course level, the ideal number of course participants per instructor (4 participants/instructor), and the specific topics and musculoskeletal pathologies to be covered. In the same manner, the group concluded that 60% to 70% of course time should be focused on hands-on sessions. Conclusion: A multinational group of MSKUS sonographers using a consensus-based questionnaire (Delphi method) established the first recommendations and guidelines for MSKUS course training in the Americas. Pan-American League of Associations for Rheumatology urges that these guidelines and recommendations be adopted in the future by both national and regional institutions in the American continent involved in the training of Rheumatologists for the performance of MSKUS.

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Emergency Medicine

Glickman, S. W., C. B. Cairns, R. M. Otero, C. W. Woods, E. L. Tsalik, R. J. Langley, J. C. van Velkinburgh, L. P. Park, L. T. Glickman, V. G. Fowler, S. F. Kingsmore and E. P. Rivers (2010). "Disease Progression in Hemodynamically Stable Patients Presenting to the Emergency Department With Sepsis." Academic Emergency Medicine 17(4): 383-390. [PDF Full-Text](#)

[Glickman, Seth W.; Cairns, Charles B.; Glickman, Lawrence T.] Univ N Carolina, Sch Med, Dept Emergency Med, Chapel Hill, NC 27515 USA. [Otero, Ronny M.; Rivers, Emanuel P.] Henry Ford Hosp, Detroit, MI 48202 USA. [Woods, Christopher W.; Tsalik, Ephraim L.; Park, Lawrence P.; Fowler, Vance G., Jr.] Duke Univ, Sch Med, Dept Med, Div Infect Dis, Durham, NC 27706 USA. [Langley, Raymond J.; van Velkinburgh, Jennifer C.; Kingsmore, Stephen F.] Natl Ctr Genome Res, Santa Fe, NM USA.

Background: Aggressive diagnosis and treatment of patients presenting to the emergency departments (ED) with septic shock has been shown to reduce mortality. To enhance the ability to intervene in patients with lesser illness severity, a better understanding of the natural history of the early progression from simple infection to more severe illness is needed. Objectives: The objectives were to 1) describe the clinical presentation of ED sepsis, including types of infection and causative microorganisms, and 2) determine the incidence, patient characteristics, and mortality associated with early progression to septic shock among ED patients with infection. Methods. This was a multicenter study of adult ED patients with sepsis but no evidence of shock. Multivariable logistic regression was used to identify patient factors for early progression to shock and its association with 30-day mortality. Results: Of 472 patients not in shock at ED presentation (systolic blood pressure > 90 mm Hg and lactate < 4 mmol/L) 84 (17.8%) progressed to shock within 72 hours. Independent factors associated with early progression to shock included older age, female sex, hyperthermia, anemia, comorbid lung disease, and vascular access device infection. Early progression to shock (vs. no progression) as associated with higher 30-day mortality (13.1% vs 3.1%, odds ratio [OR] = 4.72, 95% confidence interval [CI] = 2.01 to 11.1; $p < 0.001$). Among 379 patients with uncomplicated sepsis (i.e., no evidence of shock or any end-organ dysfunction), 86 (22.7%) progressed to severe sepsis or shock within 72 hours of hospital admission. Conclusions: A significant portion of ED patients with less severe sepsis progress to severe sepsis or shock within 72 hours. Additional diagnostic approaches are needed to risk stratify and more effectively treat ED patients with sepsis. *ACADEMIC EMERGENCY MEDICINE* 2010; 17:383-390 (C) 2010 by the Society for Academic Emergency Medicine.

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Emergency Medicine

Prendergast, H. M., D. Jurivich, M. Edison, E. B. Bunney, J. Williams and A. Schlichting (2010). "Preparing the Front Line for the Increase in the Aging Population: Geriatric Curriculum Development for an Emergency Medicine Residency Program." *Journal of Emergency Medicine* 38(3): 386-392. [PDF Full-Text](#)

[Prendergast, Heather M.; Edison, Marcia; Bunney, E. Bradshaw; Williams, John] Univ Illinois, Dept Emergency Med, Med Ctr, Chicago, IL 60612 USA. [Jurivich, Donald] Univ Illinois, Sect Geriatr, Dept Med, Med Ctr, Chicago, IL USA. [Edison, Marcia] Univ Illinois, Dept Med Educ, Med Ctr, Chicago, IL USA. [Schlichting, Adam] Henry Ford Med Ctr, Dept Emergency Med, Detroit, MI USA. Prendergast, HM, Univ Illinois, Dept Emergency Med, Med Ctr, 808 S Wood St, Room 471-H CME, Chicago, IL 60612 USA.

Background: Emergency Departments (EDs) are common entry points to the health care system for elders. Emergency Medicine residents need specialized education about geriatric patients to maximize health outcomes. Objectives: To determine whether geriatric education provided to residents in Emergency Medicine results in improved knowledge of and attitudes toward geriatric patients. Method: A pre- and post-intervention survey was conducted in a 3-year university-based residency program in Emergency Medicine. Participants were Emergency Medicine residents (PGY 1-3). The curriculum "Care of the Aging Patient in Emergency Medicine" was introduced. Topic selection was based upon geriatric curriculum recommendations and resident surveys. Before starting the curriculum and at its conclusion, residents completed Geriatric Clinical Decision-making Assessments and the Geriatric Attitude Scale Survey. Pre- and post-assessments were compared. Residents also completed written assessments for each educational activity in the curriculum. Results: After participating in the program, residents demonstrated improved knowledge of the geriatric patient, and their attitudes toward caring for geriatric patients had shifted from negative to neutral or positive. One statistically relevant change centered on the item, "Taking a medical history from an elderly patient is an ordeal" ($p = 0.033$) Pre-intervention, 8.3% ($n = 3$) of residents strongly agreed with the statement. After the intervention, strong disagreement with the statement increased from 2.8% ($n = 1$) to 11% ($n = 4$) on the educational surveys. In addition, an increase in the percentage of neutral responses was observed. Conclusions: Using familiar educational formats with heavy emphasis on "hands-on" activities to present the geriatric care curriculum had a positive impact on resident knowledge and confidence in dealing with geriatric patients. Published by Elsevier Inc.

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Emergency Medicine

Tsalik, E. L., D. Jones, B. Nicholson, L. Waring, O. Liesenfeld, L. P. Park, S. W. Glickman, L. B. Caram, R. J. Langley, J. C. van Velkinburgh, C. B. Cairns, E. P. Rivers, R. M. Otero, S. F. Kingsmore, T. Lalani, V. G. Fowler and C. W. Woods (2010). "Multiplex PCR To Diagnose Bloodstream Infections in Patients Admitted from the Emergency Department with Sepsis." Journal of Clinical Microbiology **48**(1): 26-33. [PDF Full-Text](#)

[Tsalik, Ephraim L.; Park, Lawrence P.; Caram, Lauren B.; Fowler, Vance G.; Woods, Christopher W.] Duke Univ, Sch Med, Dept Med, Div Infect Dis, Durham, NC 27706 USA. [Jones, Daphne; Nicholson, Bradly] Durham VA Med Ctr, Dept Med, Durham, NC USA. [Glickman, Seth W.; Cairns, Charles B.] Univ N Carolina, Sch Med, Dept Emergency Med, Chapel Hill, NC USA. [Rivers, Emanuel P.; Otero, Ronny M.] Wayne State Univ, Henry Ford Hosp, Detroit, MI USA. [Langley, Raymond J.; van Velkinburgh, Jennifer C.; Kingsmore, Stephen F.] Natl Ctr Genome Resources, Santa Fe, NM USA. [Lalani, Tahaniyat] USN, Med Ctr, Portsmouth, VA USA. [Waring, Lynette; Liesenfeld, Oliver] Roche Mol Diagnost, Pleasanton, CA USA. Woods, CW, Dept Vet Affairs 111H, 508 Fulton St, Durham, NC 27705 USA. woods004@mc.duke.edu

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

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Gastroenterology

Wu, I. C., C. L. Lai, S. H. B. Han, K. H. Han, S. C. Gordon, Y. C. Chao, C. K. Tan, W. Sievert, T. Tanwandee, D. Xu, B. L. Neo and T. T. Chang (2010). "Efficacy of Entecavir in Chronic Hepatitis B Patients with Mildly Elevated Alanine Aminotransferase and Biopsy-Proven Histological Damage." Hepatology **51**(4): 1185-1189. [PDF Full-Text](#)

[Chang, Ting-Tsung] Natl Cheng Kung Univ Hosp, Dept Internal Med, Tainan 704, Taiwan. [Wu, I-Chin; Chang, Ting-Tsung] Natl Cheng Kung Univ, Coll Med, Inst Clin Med, Tainan 70101, Taiwan. [Lai, Ching-Lung] Univ Hong Kong, Queen Mary Hosp, Hong Kong, Hong Kong, Peoples R China. [Han, Steven-Huy Bui] Univ Calif Los Angeles, Sch Med, Los Angeles, CA USA. [Han, Kwang-Hyup] Yonsei Univ, Coll Med, Severance Hosp, Seoul, South Korea. [Gordon, Stuart C.] Henry Ford Hosp, Detroit, MI 48202 USA. [Chao, You-Chen] Tri Serv Gen Hosp, Taipei, Taiwan. [Tan, Chee-Kiat] Singapore Gen Hosp, Singapore 0316, Singapore. [Sievert, William] Monash Univ, Dept Med, Monash Med Ctr, Melbourne, Vic 3004, Australia. [Tanwandee, Tawesak] Siriraj Hosp, Bangkok, Thailand. [Xu, Dong] Bristol Myers Squibb Co, Res & Dev, Wallingford, CT 06492 USA. [Neo, Boon-Leong] Bristol Myers Squibb Co, Res & Dev, Singapore, Singapore. Chang, TT, Natl Cheng Kung Univ Hosp, Dept Internal Med, 138 Sheng Li Rd, Tainan 704, Taiwan. ttchang@mail.ncku.edu.tw

Current guidelines for management of chronic hepatitis B recommend treatment for patients presenting with elevated hepatitis B virus (HBV) DNA and alanine aminotransferase (ALT) >2 X upper limit of normal (ULN) or histological evidence of liver disease. Retrospective analyses have demonstrated that significant hepatic necroinflammation and fibrosis were present in a substantial proportion of patients with ALT 1 to 2 x ULN. To assess therapeutic efficacy in this clinical setting, we retrospectively examined treatment endpoints among the subset of nucleoside-naive chronic hepatitis B (CHB) patients treated in phase 3 clinical trials of entecavir who

had both screening and baseline serum ALT 1.3 to 2 x ULN. A total of 1347 patients were randomized to treatment with entecavir or lamivudine. Three hundred thirty-six patients, constituting 25% of the total study population, had screening and baseline ALT 1.3 to 2 x ULN. Clinically significant necroinflammation (Knodell necroinflammation score ≥ 7) was observed in 60% and 72% of hepatitis B e antigen (HBeAg)-positive and HBeAg-negative patients, respectively, whereas marked fibrosis (Ishak fibrosis score ≥ 4) was observed in 8% and 15% of HBeAg-positive and HBeAg-negative patients, respectively. Among entecavir-treated HBeAg-negative patients, the proportions of patients achieving histological improvement, HBV DNA <300 copies/mL, and ALT normalization were similar between patients with mildly elevated ALT and those with ALT >2 x ULN. However, entecavir-treated HBeAg-positive patients with mildly elevated ALT had lower response rates for histological improvement, HBV DNA less than 300 copies/mL, ALT normalization, and HBeAg seroconversion than those with ALT greater than 2 X ULN. Conclusion: This retrospective analysis demonstrated that HBeAg-negative CHB patients treated with entecavir responded similarly irrespective of baseline ALT level. However, HBeAg-positive patients with mildly elevated ALT responded less well to treatment with entecavir than did those with ALT greater than 2 x ULN. (HEPATOLOGY 2010;51:1185-1189.)

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Health Enhancement Center

Saval, M. A., D. J. Kerrigan, K. M. Ophaug, J. K. Ehrman and S. J. Keteyian (2010). "Relationship Between Leg Muscle Endurance and $(\dot{V} \text{ over } \dot{E}/(\dot{V} \text{ over } \dot{CO}_2))$ Slope in Patients With Heart Failure." Journal of Cardiopulmonary Rehabilitation and Prevention **30**(2): 106-110. [PDF Full-Text](#)

[Saval, Matthew A.; Kerrigan, Dennis J.; Ehrman, Jonathan K.; Keteyian, Steven J.] Henry Ford Hosp, Detroit, MI 48202 USA. [Ophaug, Kristin M.] Wayne State Univ, Detroit, MI USA.
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PURPOSE: Ventilatory efficiency, as measured by the slope of the relationship between minute ventilation and carbon dioxide production $(\dot{V} \text{ over } \dot{E}/(\dot{V} \text{ over } \dot{CO}_2))$ slope) during cardiopulmonary exercise (CPX) testing, is an important prognostic measure in patients with heart failure (HF). An abnormal slope is linked to the skeletal muscle metaboreflex. In addition, skeletal muscle endurance is reduced in patients with HF. However, the relationship between $(\dot{V} \text{ over } \dot{E}/(\dot{V} \text{ over } \dot{CO}_2))$ slope and skeletal muscle endurance is not known. This investigation tests the hypothesis that reduced knee extensor muscle endurance is inversely related to an elevated $(\dot{V} \text{ over } \dot{E}/(\dot{V} \text{ over } \dot{CO}_2))$ slope during CPX testing in patients with HF and that these variables are not related in normal subjects. **METHODS:** Patients with HF (n = 32) and 6 age-matched normal subjects performed CPX testing and isokinetic dynamometry to determine the $(\dot{V} \text{ over } \dot{E}/(\dot{V} \text{ over } \dot{CO}_2))$ slope and knee extensor muscle endurance, respectively. **RESULTS:** The $(\dot{V} \text{ over } \dot{E}/(\dot{V} \text{ over } \dot{CO}_2))$ slope and leg muscle endurance percentage were significantly related in patients with HF (r = -0.68, P < .001), but not in normal subjects (r = -0.11, P = .83). **DISCUSSION:** Based on these data, abnormalities of skeletal muscle endurance of patients with HF partially account for $(r^2) = 0.46$; standard error estimate = 6.6) abnormalities of ventilatory efficiency, as measured by the $(\dot{V} \text{ over } \dot{E}/(\dot{V} \text{ over } \dot{CO}_2))$ slope. This finding helps explain, in part, the factors that influence an established prognostic indicator, elevated $(\dot{V} \text{ over } \dot{E}/(\dot{V} \text{ over } \dot{CO}_2))$ slope. Future research is needed to determine whether the relationship between skeletal muscle dysfunction and ventilatory efficiency is directly mediated through the skeletal muscle ergoreflex.

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Hematology, Medical Oncology & Josephine Ford Cancer Center

Zuberi, L., A. Adeyinka and P. Kuriakose (2010). "Rapid response to induction in a case of acute promyelocytic leukemia with MYC amplification on double minutes at diagnosis." Cancer Genetics and Cytogenetics **198**(2): 170-172. [Article Request Form](#)

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Hypertension & Vascular Research

Wang, F. F., Q. He, Y. Sun, X. G. Dai and X. P. Yang (2010). "Female Adult Mouse Cardiomyocytes Are Protected Against Oxidative Stress." Hypertension **55**(5): 1172-U166. [PDF Full-Text](#)

[Wang, Fangfei; He, Quan; Sun, Ying; Dai, Xiangguo; Yang, Xiao-Ping] Henry Ford Hosp, Hypertens & Vasc Res Div, Dept Internal Med, Detroit, MI 48202 USA. [Sun, Ying] N China Coal Med Coll, Dept Pathol, Tangshan, Peoples R China.

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Pre-menopausal women have less cardiovascular disease and lower cardiovascular morbidity and mortality than men the same age. Our previous studies showed that female mice have lower mortality and better preserved cardiac function after myocardial infarction. However, the precise cellular and molecular mechanisms responsible for such a sex difference are not well established. Using cultured adult mouse cardiomyocytes, we tested the hypothesis that the survival advantage of females stems from activated estrogen receptors and Akt survival signaling pathways. Adult mouse cardiomyocytes were isolated from male and female C57BL/6J mice and treated with hydrogen peroxide (100 μ mol/E) for 30 minutes. Cell survival was indicated by rod ratio (rod shaped cells:total cells), cell death by lactate dehydrogenase release, and positive staining of annexin-V (a marker for apoptosis) and propidium iodide (a marker for necrosis). In response to hydrogen peroxide, female adult mouse cardiomyocytes exhibited a higher rod ratio, lower lactate dehydrogenase release, and fewer Annexin-V positive and propidium iodide positive cells compared with males. Phospho-Akt was greater in females both at baseline and after hydrogen peroxide stimulation. The downstream molecule of Akt, phosphor GSK-30 (inactivation), was also higher, whereas caspase 3 activity was lower in females in response to hydrogen peroxide. Bcl-2 did not differ between sexes. Estrogen receptor- α was the dominant isoform in females, whereas estrogen receptor- β was low but similar in both sexes. Our findings demonstrate that female adult mouse cardiomyocytes have a greater survival advantage when challenged with oxidative stress induced cell death. This may be attributable to activation of Akt and inhibition of GSK-30 and caspase 3 through an estrogen receptor- α mediated mechanism. (Hypertension. 2010;55:1172-1178.)

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Infectious Diseases

Aguilar, J., V. Urdy-Cornejo, S. Donabedian, M. Perri, R. Tibbetts and M. Zervos (2010). "Staphylococcus aureus Meningitis Case Series and Literature Review." Medicine **89**(2): 117-125. [PDF Full-Text](#)

[Aguilar, Javier; Urdy-Cornejo, Varinia; Donabedian, Susan; Perri, Mary; Tibbetts, Robert; Zervos, Marcus] Henry Ford Hosp, Div Infect Dis & Microbiol, Detroit, MI 48202 USA. [Zervos, Marcus] Wayne State Univ, Sch Med, Detroit, MI USA.

Aguilar, J, Henry Ford Hosp, Div Infect Dis, 2799 W Grand Blvd, CFP-304, Detroit, MI 48202 USA. jaquila1@hfhs.org

Staphylococcus aureus meningitis is a challenging disease and little is known about its epidemiology. There are no established management guidelines. We retrospectively reviewed the clinical information, bacteriologic data, and outcomes of all 33 patients with cerebrospinal fluid (CSF) cultures positive for S aureus seen at a single urban teaching hospital from 1999 to 2008. Pulsed-field gel electrophoresis (PFGE) and polymerase chain reaction for staphylococcal cassette chromosome mec (SCCmec), accessory gene regulator (agr) typing, and Panton-Valentine leukocidin (PVL) loci were done on methicillin-resistant S aureus (MRSA) CSF isolates starting in 2005. S aureus caused 12 (36%) cases of postoperative and 21 (64%) cases of hematogenous meningitis. MRSA isolates were found in 6 (50%) cases of postoperative and 10 (48%) cases of hematogenous meningitis. Twelve (75%) of the 16 MRSA infections occurred in the last 5 years of the study. Hematogenous meningitis was associated with older age ($p = 0.04$), injection drug use ($p < 0.01$), community-acquired infection ($p < 0.01$), underlying disease ($p = 0.01$), staphylococcal infection outside the central nervous system ($p = 0.01$), altered mental status ($p = 0.02$), fever ($p = 0.01$), septic shock ($p = 0.03$), and bacteremia ($p < 0.01$). The analysis of the 9 MRSA isolates showed 3 PFGE types: 3 USA100 (33%), 5 USA300 (56%), and 1 USANot100-1100 (11%). For SCCmec typing, there were 2 (22%) type II and 7 (78%) type IV. All USA300 strains were SCCmec IVa. For agr typing, there were 5 (56%) type I and 4 (44%) type II. Three isolates (33%) were positive for the PVL gene and were USA300 strains. Most patients received nafcillin or vancomycin with or without rifampin or trimethoprim/sulfamethoxazole for a mean period of 17 days (range, 1-42 d). Overall mortality was 36%, and it was associated with community-acquired infection ($p = 0.02$).

Postoperative and hematogenous *S aureus* meningitis are distinct clinical syndromes. *S aureus* hematogenous meningitis has devastating clinical consequences and elevated mortality rates, especially if it is acquired in the community. The incidence of MRSA meningitis increased over the last 5 years of the study. Treatment of choice is nafcillin for methicillin-sensitive strains and vancomycin for MRSA strains. The addition of trimethoprim/sulfamethoxazole or rifampin to vancomycin is recommended in severe cases and community-acquired MRSA infections. Linezolid is also a good option due to its good CSF penetration and favorable case reports. The mortality rate is higher in infections acquired in the community.

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Internal Medicine

Kaatz, S. (2010). "What you should know about the 2008 American College of Chest Physicians evidence-based clinical practice guidelines (8th) on antithrombotic and thrombolytic therapy." J Thromb Thrombolysis **29**(2): 219-26. [PDF Full-Text](#)

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The American College of Chest Physicians published their first consensus conference guidelines on antithrombotic therapy in 1986 and has updated these guidelines approximately every 3 years as a supplement to the journal *Chest*. These guidelines are widely accepted as an authoritative source of information and considered by many to be the textbook for antithrombotic therapy. The most recent guidelines are from the 8th consensus conference, published in 2008, and this article will highlight new recommendations that have evolved since the 2004 *Chest* supplement. Examples from the literature that support the evolution these guidelines will focus on changes that are most germane to the majority of attendees at the 10th National Conference on Anticoagulant Therapy and members of the AC Forum. The objective of this article is to help answer ten common clinical questions frequently faced by anticoagulation management services.

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Internal Medicine

Kaatz, S. (2010). "Impact on patient care: patient case through the continuum of care." J Thromb Thrombolysis **29**(2): 167-70. [PDF Full-Text](#)

Henry Ford Hospital, General Internal Medicine, 2799 W. Grand Blvd, Detroit, MI 48202, USA. skaatz1@hfhs.org

Hospitalized patients are at increased risk of venous thromboembolism and the Joint Commission has initiated practice measures to improve the rates of preventable events. The Joint Commission also initiated the National Patient Safety Goals for medication prescribing and administration, of which, goal 03.05.01 is specifically aimed at anticoagulation therapy. These measures and goals are consistent with the American College of Chest Physicians' Consensus Guidelines on Antithrombotic and Thrombolytic Therapy. This narrative review uses a case-based approach that brings up practical clinical questions regarding these measures, goals and guidelines as they apply to a patient going through the continuum of care from the hospital to their home.

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Nephrology

Plantinga, L. C., D. C. Crews, J. Coresh, E. R. Miller, R. Saran, J. Yee, E. Hedgeman, M. Paykov, M. S. Eberhardt, D. E. Williams and N. R. Powe (2010). "Prevalence of Chronic Kidney Disease in US Adults with Undiagnosed Diabetes or Prediabetes." Clinical Journal of the American Society of Nephrology **5**(4): 673-682. [PDF Full-Text](#)

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Background and objectives: Prevalence of chronic kidney disease (CKD) in people with diagnosed diabetes is known to be high, but little is known about the prevalence of CKD in those with undiagnosed diabetes or prediabetes. We aimed to estimate and compare the community prevalence of CKD among people with diagnosed diabetes, undiagnosed diabetes, prediabetes, or no diabetes. Design, setting, participants, & measurements: The 1999 through 2006 National Health and Nutrition Examination Survey is a representative survey of the civilian, noninstitutionalized US population. Participants who were aged ≥ 20 years; responded to the diabetes questionnaire; and had fasting plasma glucose (FPG), serum creatinine, and urinary albumin-creatinine ratio measurements were included (N = 8188). Diabetes status was defined as follows: Diagnosed diabetes, self-reported provider diagnosis (n = 826); undiagnosed diabetes, FPG ≥ 126 mg/dl without self-reported diagnosis (n = 299); prediabetes, FPG ≥ 100 and <126 mg/dl (n = 2272); and no diabetes, FPG <100 mg/dl (n = 4791). Prevalence of CKD was defined by estimated GFR 15 to 59 ml/min per 1.73 m² or albumin-creatinine ratio ≥ 30 mg/g; adjustment was performed with multivariable logistic regression. Results: Fully 39.6% of people with diagnosed and 41.7% with undiagnosed diabetes had CKD; 17.7% with prediabetes and 10.6% without diabetes had CKD. Age-, gender-, and race/ethnicity-adjusted prevalence of CKD was 32.9, 24.2, 17.1, and 11.8%, for diagnosed, undiagnosed, pre-, and no diabetes, respectively. Among those with CKD, 39.1% had undiagnosed or prediabetes. Conclusions: CKD prevalence is high among people with undiagnosed diabetes and prediabetes. These individuals might benefit from interventions aimed at preventing development and/or progression of both CKD and diabetes. Clin J Am Soc Nephrol 5: 673-682, 2010. doi: 10.2215/CJN.07891109

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Nephrology

Sandhu, A., S. Soman, M. Hudson and A. Besarab (2010). "Managing anemia in patients with chronic heart failure: what do we know?" Vasc Health Risk Manag **6**: 237-52. 2856579. [PDF Full-Text](#)

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Anemia is common in patients with chronic heart failure (HF) with an incidence ranging from 4% to 55% depending on the studied population. Several studies have highlighted that the prevalence of anemia increases with worsening heart failure as reflected by New York Heart Association classification. Additionally, several epidemiological studies have highlighted its role as a prognostic marker, linking it to worse outcomes including; malnutrition, increased hospitalizations, refractory heart failure and death. The pathophysiology of anemia is multifactorial and related to various factors including; hemodilution, iron losses from anti-platelet drugs, activation of the inflammatory cascade, urinary losses of erythropoietin and associated renal insufficiency. There are a host of epidemiological studies examining HF outcomes and anemia, but only a few randomized trials addressing this issue. The purpose of this article is to review the literature that examines the interrelationship of anemia and congestive HF, analyzing its etiology, impact on outcomes and also the role of associated kidney disease as well as cardiorenal syndrome both as a marker of morbidity and mortality.

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Neurology

Friedman, H. S., M. D. Prados, P. Y. Wen, T. Mikkelsen, D. Schiff, L. E. Abrey, W. K. A. Yung, N. Paleologos, M. K. Nicholas, R. Jensen, J. Vredenburgh, J. Huang, M. X. Zheng and T. Cloughesy (2010). "Bevacizumab and Recurrent Malignant Gliomas: A European Perspective Reply." Journal of Clinical Oncology **28**(12): E190-E192. [PDF Full-Text](#)

[Friedman, Henry S.] Duke Univ, Preston Robert Tisch Brain Tumor Ctr Duke, Durham, NC 27710 USA. [Prados, Michael D.] Univ Calif San Francisco, Dept Neurosurg, San Francisco, CA 94143 USA. [Wen, Patrick Y.] Brigham & Womens Hosp, Dept Neurol, Boston, MA 02115 USA. [Wen, Patrick Y.] Dana Farber Canc Inst, Ctr Neurooncol, Boston, MA 02115 USA. [Mikkelsen, Tom] Henry Ford Hosp, Hermelin Brain Tumor Ctr, Detroit, MI 48202 USA. [Schiff, David] Univ Virginia, Dept Neurol, Charlottesville, VA USA. [Abrey, Lauren E.] Mem Sloan Kettering Canc Ctr, Dept Neurol, New York, NY 10021 USA. [Yung, W. K. Alfred] Univ Texas MD Anderson Canc Ctr, Dept Neurooncol, Houston, TX 77030 USA. [Paleologos, Nina] NorthShore Univ Hlth Syst, Dept Neurol, Evanston, IL USA. [Nicholas, Martin K.] Univ Chicago, Dept Neurol, Chicago, IL 60637 USA. [Jensen, Randy] Univ Utah Hosp, Salt Lake City, UT USA. [Vredenburgh, James] Duke Univ, Preston Robert

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Neurology

Xu, J., X. F. Liu, J. L. Chen, A. Zacharek, X. Cui, S. Savant-Bhonsale, M. Chopp and Z. G. Liu (2010). "Cell-Cell Interaction Promotes Rat Marrow Stromal Cell Differentiation Into Endothelial Cell via Activation of TACE/TNF-alpha Signaling." Cell Transplantation **19**(1): 43-53. [PDF Full-Text](#)

[Xu, Jian; Liu, Zhenguo] Ohio State Univ, Med Ctr, Davis Heart & Lung Res Inst, Columbus, OH 43210 USA. [Xu, Jian; Liu, Xinfeng] Nanjing Univ, Sch Med, Jinling Hosp, Dept Neurol, Nanjing 210008, Peoples R China. [Xu, Jian; Chen, Jieli; Zacharek, Alex; Cui, Xu; Chopp, Michael] Henry Ford Hlth Sci Ctr, Dept Neurol, Detroit, MI USA. [Savant-Bhonsale, Smita] Theradigm Inc, Baltimore, MD USA. [Chopp, Michael] Oakland Univ, Dept Phys, Rochester, MI USA.

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Marrow stromal cells (MSCs) are capable of differentiating into various cell types including endothelial cells. Microenvironment is important in cell fate determination. Tumor necrosis factor- α converting enzyme (TACE), a well-characterized "sheddase," participates in the differentiation process of multiple lineages by the proteolytic release of membrane-bound proteins such as tumor necrosis factor- α (TNF- α). We investigated the endothelial differentiation of MSCs under two coculture conditions: 1) direct MSCs-rat brain microvascular endothelial cells (rBMECs) contact coculture; and 2) indirect coculture of MSCs and rBMECs. Also, we examined the role of TACE/TNF- α signaling in the process of differentiation under direct coculture condition. We found that endothelial differentiation of MSCs was substantially enhanced in MSCs-rBMECs direct contact coculture, but not in indirect transwell coculture condition. Transcript levels of TACE and TNF- α as well as TACE protein expression were significantly upregulated in direct, but not in indirect, coculture condition. Addition of human recombinant TACE promoted gene expression of endothelial specific markers including vWF, CD31, VE-cadherin, Flk-1, and Flt-1 in the differentiating MSCs. Furthermore, inhibition of TACE with TAPI-2 or inhibition of TNF- α with Etanercept attenuated endothelial differentiation of MSCs in the direct coculture condition. We demonstrated for the first time that direct MSCs-rBMECs interaction stimulated the endothelial differentiation of MSCs via TACE/TNF α signaling.

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Neurology

Zhou, G. Y., S. Ge, D. Z. Liu, G. L. Xu, R. L. Zhang, Q. Yin, W. S. Zhu, J. L. Chen and X. F. Liu (2010). "Atorvastatin Reduces Plaque Vulnerability in an Atherosclerotic Rabbit Model by Altering the 5-Lipoxygenase Pathway." Cardiology **115**(3): 221-228. [Article Request Form](#)

[Zhou, Guangyi; Ge, Song; Liu, Dezhi; Xu, Gelin; Zhang, Renliang; Yin, Qin; Zhu, Wusheng; Liu, Xinfeng] Nanjing Univ, Dept Neurol, Jinling Hosp, Sch Med, Nanjing 210002, Jiangsu Prov, Peoples R China. [Chen, Jieli] Henry Ford Hosp, Dept Neurol, Detroit, MI 48202 USA.

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Objective: The 5-lipoxygenase catalyzed formation of leukotriene lipid mediators is a mediator for inflammatory response in arteries. The present study investigated the relationship between atorvastatin and the 5-lipoxygenase pathway in an atherosclerotic rabbit model. Methods: Thirty male New Zealand White Rabbits were randomized into negative control, positive control and atorvastatin groups. At week 4, the rabbits were subjected to carotid balloon-dilation injury or carotid balloon-dilation injury, followed by treatment with atorvastatin. At week 12, all the animals were sacrificed. Plasma lipids, LTD4, and 15-epi-lipoxin A(4) were measured using the enzymatic endpoint method and ELISA, respectively. RT-PCR was performed to detect the gene expression of 5-lipoxygenase-activating protein and cysLT1R in rabbit carotid arteries. Finally, histological analysis was used to evaluate the pathophysiological changes of rabbit carotid arteries. Results: The results showed atorvastatin markedly lowered serum lipids and LTD4 levels compared with the control

group. Similarly, mRNA expression of 5-lipoxygenase-activating protein and cysLT1R was significantly inhibited by atorvastatin. Decreased carotid plaque instability was evident in atorvastatin-treated animals, as demonstrated by a thickened elastic layer, less neointima hyperplasia and macrophage proliferation. Conclusions: Atorvastatin may stabilize carotid plaque by regulating the 5-lipoxygenase pathway in atherosclerotic rabbits and delay the progression of atherosclerosis by exerting anti-inflammatory effects. Copyright (C) 2010 S. Karger AG, Basel

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Neurosurgery

Kaufman, C. B., J. W. Mink and J. M. Schwalb (2010). "Bilateral deep brain stimulation for treatment of medically refractory paroxysmal nonkinesigenic dyskinesia Case report." Journal of Neurosurgery **112**(4): 847-850. [PDF Full-Text](#)

[Schwalb, Jason M.] Henry Ford Hlth Syst, Dept Neurosurg, Detroit, MI 48202 USA. [Kaufman, Christian B.] Univ Rochester, Dept Neurosurg, New York, NY USA. [Mink, Jonathan W.] Univ Rochester, Dept Neurol, New York, NY USA.

Schwalb, JM, Henry Ford Hlth Syst, Dept Neurosurg, 2799 W Grand Blvd,K-11, Detroit, MI 48202 USA. JSCHWAL1@hfhs.org

The authors present the case of a 26-year-old man with a 10-15-year history of worsening bilateral dystonia and baseline chorea occurring up to 20 times per day that was exacerbated by stress and anxiety and was refractory to medical management. Paroxysmal nonkinesigenic dyskinesia was diagnosed, which is a rare hyperkinetic movement disorder that is episodic and does not respond to nonbenzodiazepine antiepileptics. The patient was significantly debilitated by his disease, lived in a group home, and suffered from frequent falls, necessitating the wearing of a protective helmet and face mask at all times. The patient underwent implantation of bilateral deep brain stimulation quadripolar electrodes in the globus pallidus internus with the aid of image-guided stereotactic neurosurgery and microelectrode recording without complication. At his 1-month postoperative follow-up, the patient reported a subjective 90% improvement in his symptoms: the only notable side effect was a slight increased slurring in his baseline dysarthria. Objective reporting and recording forms maintained by the patient's caretakers over the following 18 months suggested a significant and sustained improvement in his overall balance, ambulation, and gross motor function with a substantial decrease in the incidence of reported falls. The authors conclude that pallidal deep brain stimulation may be successfully applied to patients suffering from refractory paroxysmal nonkinesigenic dyskinesia with promising results. This treatment strategy deserves further prospective investigation. clinical consideration. and refinement. (DOI: 10.3171/2009.9.JNS09454)

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Otolaryngology

Rossmiller, S. R., S. B. Cannady, T. A. Ghanem and M. K. Wax (2010). "Transfusion criteria in free flap surgery." Otolaryngology-Head and Neck Surgery **142**(3): 359-364. [PDF Full-Text](#)

[Rossmiller, Sarah R.; Wax, Mark K.] Oregon Hlth & Sci Univ, Dept Otolaryngol Head & Neck Surg, Portland, OR 97201 USA. [Cannady, Steven B.] Head & Neck Ctr, Rochester, NY USA. [Ghanem, Tamer A.] Henry Ford Hlth Syst, Dept Otolaryngol Head & Neck Surg, Detroit, MI USA.

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OBJECTIVE: The ideal hematocrit for patients undergoing free flap reconstruction is unknown. It is standard practice to keep hematocrit levels above 30 percent, although there is evidence that blood transfusions are associated with both infectious and noninfectious complications. We propose that lowering the trigger for postoperative transfusions from 30 percent to 25 percent will not increase flap-related complications and may reduce unnecessary blood transfusions. **STUDY DESIGN:** Observational cohort study. **SETTING:** Tertiary care center. **SUBJECTS AND METHODS:** Patients undergoing free tissue transfer from January 2007 through February 2008 received blood transfusions for hematocrit < 30 percent, whereas patients having surgery from March 2008 through April 2009 received blood transfusions for hematocrit < 25 percent. Outcomes include flap-related complications, length of stay, number of units transfused, and lowest postoperative hematocrit. **RESULTS:** In the group transfused for hematocrit < 30 percent, 123 patients underwent 129 free flaps. In the group transfused for hematocrit < 25 percent, 122 patients underwent 135 flaps. The mean lowest postoperative hematocrit levels were significantly lower in the group transfused for hematocrit < 25 percent

compared with the group transfused for hematocrit < 30 percent (26.6% vs 28.4%, respectively, P < 0.0001). The group with hematocrit < 25 percent also received fewer units of blood transfused (1.47 vs 2.11, P = 0.028). Complication rates between the two groups were not significantly different aside from higher rates of fistula and respiratory failure in the group transfused for hematocrit < 30 percent. Flap loss was 2.3 percent compared with 6.7 percent (P = 0.138). CONCLUSION: For patients undergoing free flap surgery, a postoperative transfusion trigger of hematocrit < 25 percent decreases blood transfusion rates without increasing rates of flap-related complications. (c) 2010 American Academy of Otolaryngology Head and Neck Surgery Foundation. All rights reserved.

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Pathology

Ali, S. and V. Shah (2010). "Small-duct primary sclerosing cholangitis with hepatocellular carcinoma requiring liver transplantation." Hepatobiliary & Pancreatic Diseases International **9**(2): 208-212. [PDF Full-Text](#)

[Ali, Sharif; Shah, Veena] Henry Ford Hlth Syst, Dept Pathol & Lab Med, Detroit, MI 48202 USA.

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BACKGROUND: Primary sclerosing cholangitis (PSC) is a chronic progressive cholestatic liver disease, which usually affects young adults and is diagnosed by cholangiography. On a few occasions, the disease either starts in or exclusively involves the small intrahepatic bile ducts, referred to as small-duct PSC. METHODS: A 31-year-old man presented with severe hematemesis secondary to liver cirrhosis. Over a course of 8 years, his liver decompensated and required an orthotopic liver transplantation. In this report we discuss his disease presentation, course of management, and the post-transplantation course of management, and review the morphologic diagnosis, and differential diagnosis of the disease with large-duct type and other diseases that involve small intrahepatic bile ducts. RESULTS: The patient's explanted liver showed changes of PSC affecting only the small- and medium-sized bile ducts in addition to three incidental nodules of hepatocellular carcinoma. CONCLUSIONS: Small-duct PSC has a substantially better prognosis than the large-duct type, with less chance of developing cirrhosis and an equal risk for developing hepatocellular carcinoma, but no increased risk for developing cholangiocarcinoma. Treatment seems to help relieve the symptoms but not necessarily improve survival. Liver transplantation remains the ultimate cure. (Hepatobiliary Pancreat Dis Int 2010; 9:208-212)

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Pathology

Salama, M. E., M. R. Mariappan, K. Inamdar, S. R. Tripp and S. L. Perkins (2010). "The Value of CD23 Expression as an Additional Marker in Distinguishing Mediastinal (Thymic) Large B-Cell Lymphoma From Hodgkin Lymphoma." International Journal of Surgical Pathology **18**(2): 121-128. [Article Request Form](#)

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Mediastinal diffuse large B-cell lymphoma (Med-DLBCL) is a subtype of DLBCL that has morphologic and clinical similarities and phenotypic overlaps with classical Hodgkin lymphoma (CHL) involving the mediastinum. CD23 is a marker that has been previously reported in Med-DLBCL and is proposed in the differential diagnosis of M-DLBCL and CHL. A panel of immunostains, including CD45, CD20, CD3, CD30, CD15, CD21, and CD23 as well as Eber was performed on Med-DLBCL and 20CHL. 23/27 Med-DLBCL (85%) were positive for CD23 (membranous) CD30 was negative in 6 and positive in 21 cases. 18 CHL cases were negative for CD23 and only 2 showed rare scattered Reed-Sternberg cells with weak cytoplasmic CD23 staining. CD23 showed a sensitivity of 85% and positive predictive value of 92%. In conclusion CD23 is a useful marker in distinguishing Med-DLBCL and CHL in mediastinal biopsies and may be helpful as an adjunct to histomorphology and other markers in the diagnosis and appropriate clinical management of these lesions.

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Pharmacy

Fleming, J. N., D. J. Taber, N. A. Weimert, M. F. Egidi, J. McGillicuddy, C. F. Bratton, A. Lin, K. D. Chavin and P. K. Baliga (2010). "Comparison of efficacy of induction therapy in low immunologic risk African-American kidney transplant recipients." Transplant International **23**(5): 500-505. [PDF Full-Text](#)

[Fleming, James N.; Taber, David J.; Weimert, Nicole A.] Med Univ S Carolina, Dept Pharm Serv, Charleston, SC 29425 USA. [Egidi, Maria F.] Med Univ S Carolina, Div Nephrol, Dept Med, Charleston, SC 29425 USA. [McGillicuddy, John; Bratton, Charles F.; Lin, Angello; Chavin, Kenneth D.; Baliga, Prabhakar K.] Med Univ S Carolina, Div Transplant, Dept Surg, Charleston, SC 29425 USA. [Fleming, James N.] Henry Ford Hosp, Dept Pharm Serv, Detroit, MI 48202 USA.
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P>African-Americans (AA) have higher acute rejection rates and poorer long-term graft survival rates when compared with non-AA. It is yet to be demonstrated that the type of induction therapy modifies outcomes in this 'high-risk' population. This retrospective analysis compares the efficacy of induction therapy [antilymphocyte antibodies (ALA) versus interleukin-2 receptor antagonists (IL-2RA)] in the AA population. Some 189 AAs were included. There was no difference in acute rejection at one year between the groups (ALA (12%) or IL-2RA (12%), $P = 0.89$). Type of induction therapy had no significant effect on death-censored ($P = 0.61$) or uncensored graft survival ($P = 0.32$). There was no difference between CMV or BK virus infections between the groups ($P = 0.14$ and 0.94 respectively). Type of induction therapy does not appear to affect acute rejection rates or long-term graft survival in low-risk AA kidney transplant recipients.

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Pharmacy

Toth, N. R., R. M. Chambers and S. L. Davis (2010). "Implementation of a care bundle for antimicrobial stewardship." Am J Health Syst Pharm **67**(9): 746-9. [PDF Full-Text](#)

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PURPOSE: The impact of an antibiotic-use care bundle on compliance with quality indicators was evaluated. **METHODS:** Patients admitted to the internal medicine or surgery floor of a tertiary care center who were receiving an anti-pseudomonal beta-lactam, vancomycin, a fluoroquinolone, linezolid, an amino-glycoside, or any combination of these agents were included in the study. The study consisted of two phases: intervention (when a stewardship pharmacist was involved in patient care) and control (when no stewardship pharmacist was involved). The stewardship pharmacist completed interventions via prospective audit and suggested changes to empirical and definitive antimicrobials, monitored patients' cultures and antimicrobial therapy daily, and provided education on the institution's antibiogram. The primary outcome measured was compliance with the care bundle's quality indicators, which included documentation of treatment rationale, collection of appropriate culture specimens according to institutional and national guidelines, appropriate empirical selection of antibiotics according to institutional and national guidelines at initiation of antibiotic therapy and deescalation, and selection of appropriate agents for definitive therapy during antimicrobial therapy. **RESULTS:** A total of 160 patients and 442 antibiotic orders were evaluated. During the intervention phase, 168 interventions were made, with an acceptance rate of 91%. The rate of appropriate deescalation rose from 72% to 90% ($p = 0.01$). Compliance with all quality indicators rose from 16% to 43% ($p < 0.001$). **CONCLUSION:** Implementation of an antimicrobial stewardship program care bundle on two patient care units was associated with improved rates of compliance with quality indicators.

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Radiation Oncology

Kim, J., R. Hammoud, D. Pradhan, H. Zhong, R. Y. Jin, B. Movsas and I. J. Chetty (2010). "Prostate Localization on Daily Cone-Beam Computed Tomography Images: Accuracy Assessment of Similarity Metrics." Int J Radiat Oncol Biol Phys **EPub Ahead of Print**. [PDF Full-Text](#)

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PURPOSE: To evaluate different similarity metrics (SM) using natural calcifications and observation-based measures to determine the most accurate prostate and seminal vesicle localization on daily cone-beam CT (CBCT) images. **METHODS AND MATERIALS:** CBCT images of 29 patients were retrospectively analyzed; 14 patients with prostate calcifications (calcification data set) and 15 patients without calcifications (no-calcification data set). Three groups of test registrations were performed. Test 1: 70 CT/CBCT pairs from calcification dataset were registered using 17 SMs (6,580 registrations) and compared using the calcification mismatch error as an endpoint. Test 2: Using the four best SMs from Test 1, 75 CT/CBCT pairs in the no-calcification data set were registered (300 registrations). Accuracy of contour overlays was ranked visually. Test 3: For the best SM from Tests 1 and 2, accuracy was estimated using 356 CT/CBCT registrations. Additionally, target expansion margins were investigated for generating registration regions of interest. **RESULTS:** Test 1-Incremental sign correlation (ISC), gradient correlation (GC), gradient difference (GD), and normalized cross correlation (NCC) showed the smallest errors ($\mu \pm \sigma$: 1.6 \pm 0.9 approximately 2.9 \pm 2.1 mm). Test 2-Two of the three reviewers ranked GC higher. Test 3-Using GC, 96% of registrations showed <3-mm error when calcifications were filtered. Errors were left/right: 0.1 \pm 0.5mm, anterior/posterior: 0.8 \pm 1.0mm, and superior/inferior: 0.5 \pm 1.1 mm. The existence of calcifications increased the success rate to 97%. Expansion margins of 4-10 mm were equally successful. **CONCLUSION:** Gradient-based SMs were most accurate. Estimated error was found to be <3 mm (1.1 mm SD) in 96% of the registrations. Results suggest that the contour expansion margin should be no less than 4 mm.

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Radiation Oncology

Movsas, B., C. J. Langer, H. J. Ross, L. Wang, R. M. Jotte, S. Feigenberg, F. Xu, C. H. Huang, M. J. Monberg and C. K. Obasaju (2010). "Randomized phase II trial of cisplatin, etoposide, and radiation followed by gemcitabine alone or by combined gemcitabine and docetaxel in stage III A/B unresectable non-small cell lung cancer." *J Thorac Oncol* **5**(5): 673-9. [PDF Full-Text](#)

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PURPOSE: Southwest Oncology Group 9504 demonstrated the feasibility and potential benefit of docetaxel consolidation after etoposide, cisplatin, and radiotherapy in patients with locally advanced non-small cell lung cancer. Our study assessed consolidation with either gemcitabine alone or with docetaxel after identical chemoradiation as used in Southwest Oncology Group 9504. **METHODS:** Patients with stage III non-small cell lung cancer and good performance status were included. Treatment consisted of concurrent cisplatin 50 mg/m on days 1 and 8 plus etoposide 50 mg/m on days 1 to 5 for two 28-day cycles plus radiotherapy (62 Gy, 2 Gy daily in 31 fractions over 7 weeks), followed by randomization to either gemcitabine 1000 mg/m on days 1 and 8 (G) or gemcitabine 1000 mg/m on days 1 and 8 plus docetaxel 75 mg/m on day 1 (GD) every 21 days for three cycles. **RESULTS:** Eighty-three patients were entered, 81 received induction therapy, and 64 were randomized (32 in each arm). Grade 3 or four events, including neutropenia (56.3% vs. 28.1%, $p = 0.03$), anemia (18.8% vs. 3.1%, $p = 0.05$), and fatigue (15.6% vs. 6.3%, $p = \text{NS}$), were more frequent with GD compared with G. Among all patients, median survival from registration was 20.8 months (95% confidence interval: 16.4-33.8), and 2-year survival was 46.7% (95% confidence interval: 35.6-57.1). From randomization, median progression-free survival was 5.4 months for G and 13.4 months for GD, and median survival was 16.1 months for G and 29.5 months for GD. Two-year survival rates were 40.6% for G and 55.7% for GD. **CONCLUSION:** The doublet, as expected, resulted in more toxicity, particularly myelosuppression and fatigue. Survival associated with the GD treatment arm of this trial exceeds that of previously reported trials.

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Radiation Oncology

Schipani, S., R. Jain, K. Shah, J. P. Rock, B. Movsas, M. Rosenblum and S. Ryu (2010). "Clinical, dosimetric, and radiographic correlation of radiation injury involving the brainstem and the medial temporal lobes following stereotactic radiotherapy for neoplasms of central skull base." *J Neurooncol* **Epub Ahead of Print**. [PDF Full-Text](#)

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Stereotactic Radiotherapy (SRT) is more commonly used for skull base tumors in conjunction with the technical development of radiation intensity modulation. Purpose of this study is to correlate clinical and radiographic characteristics of delayed radiation injury (RI) occurring around central skull base following SRT with SRT dosimetric data. Total of six patients were identified to have developed RI in the vicinity of SRT target volume out of 141 patients who received SRT in the center or near-center of the skull base. The images and medical records were retrospectively reviewed. The analysis was performed for RI location, time of development, imaging and clinical characteristics and evolution of RI and correlated with SRT dosimetric analysis using image fusion with follow-up MRI scans. Mean follow-up time was 24 +/- 9 months. During the follow-up period, twelve sites of RI were found in 6 patients. They were clinically symptomatic in 4/6 patients (66.6%) at median 12.5 months after SRT. Mean time interval between SRT and detection of RI was 9 +/- 3, 18.5 +/- 5, and 13.5 months for brainstem, temporal lobe, and cerebellum/labyrinth lesions, respectively. All RI lesions were included in the region of high SRT doses. After steroid and symptomatic treatment, 50% of RI lesions showed complete response, and 40% showed partial response. RI can occur around the skull base because of irregular shape of target tumor, its close proximity to normal brain parenchyma, and inhomogeneity of dose distribution. Brainstem lesions occurred earlier than temporal lobe RI. The majority of the RI lesions, not mixed with the tumor in this study, showed radiographic and clinical improvement with steroid and symptomatic treatments.

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Radiation Oncology

Williams, J. P., S. L. Brown, G. E. Georges, M. Hauer-Jensen, R. P. Hill, A. K. Huser, D. G. Kirsch, T. J. MacVittie, K. A. Mason, M. M. Medhora, J. E. Moulder, P. Okunieff, M. F. Otterson, M. E. Robbins, J. B. Smathers and W. H. McBride (2010). "Animal Models for Medical Countermeasures to Radiation Exposure." Radiation Research **173**(4): 557-578.

[PDF Full-Text](#)

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Since September 11, 2001, there has been the recognition of a plausible threat from acts of terrorism, including radiological or nuclear attacks. A network of Centers for Medical Countermeasures against Radiation (CMCRs) has been established across the U.S.; one of the missions of this network is to identify and develop mitigating agents that can be used to treat the civilian population after a radiological event. The development of such agents requires comparison of data from many sources and accumulation of information consistent with the "Animal Rule" from the Food and Drug Administration (FDA). Given the necessity for a consensus on appropriate animal model use across the network to allow for comparative studies to be performed across institutions, and to identify pivotal studies and facilitate FDA approval, in early 2008, investigators from each of the CMCRs organized and met for an Animal Models Workshop. Working groups deliberated and discussed the wide range of animal models available for assessing agent efficacy in a number of relevant tissues and organs, including the immune and hematopoietic systems, gastrointestinal tract, lung, kidney and skin. Discussions covered the most appropriate species and strains available as well as other factors that may affect differential findings between groups and institutions. This report provides the workshop findings. (C) 2010 by Radiation Research Society

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Sleep Medicine

Ohayon, M. M., A. Krystal, T. A. Roehrs, T. Roth and M. V. Vitiello (2010). "Using difficulty resuming sleep to define nocturnal awakenings." [Sleep Medicine](#) **11**(3): 236-241. [PDF Full-Text](#)

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Objective: Nocturnal awakenings are one of the most prevalent sleep disturbances in the general population. Little is known, however, about the frequency of these episodes and how difficulty resuming sleep once awakened affects subjective sleep quality and quantity. **Method:** This is a cross-sectional telephone study with a representative sample consisting of 8937 non-institutionalized individuals aged 18 or over living in Texas, New York and California. The interviews included questions on sleeping habits, health, sleep and mental disorders. Nocturnal awakenings were evaluated according to their frequency per week and per night, as well as their duration. **Results:** A total of 35.5% of the sample reported awakening at least three nights per week. Of this 35.5%, 43%(15.2% of the total sample) reported difficulty resuming sleep once awakened. More than 80% of subjects with insomnia symptoms (difficulty initiating or maintaining sleep or non-restorative sleep) also had nocturnal awakenings. Difficulty resuming sleep was associated with subjective shorter sleep duration, poorer sleep quality, greater daytime impairment, greater consultations for sleep disturbances and greater likelihood of receiving a sleep medication. **Conclusions:** Nocturnal awakenings disrupt the sleep of about one-third of the general population. Using difficulty resuming sleep identifies individuals with significant daytime impairment who are most likely to seek medical help for their sleep disturbances. In the absence of other insomnia symptoms, nocturnal awakenings alone are unlikely to be associated with daytime impairments. (C) 2009 Elsevier B.V. All rights reserved.

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Sleep Medicine

Roth, T., G. Zammit, A. Lankford, D. Mayleben, T. Stern, V. Pitman, D. Clark and J. L. Werth (2010). "Nonrestorative Sleep as a Distinct Component of Insomnia." [Sleep](#) **33**(4): 449-458. [PDF Full-Text](#)

[Roth, Thomas] Henry Ford Hosp, Sleep Ctr, Detroit, MI 48202 USA. [Zammit, Gary] Clinilabs, New York, NY USA. [Lankford, Alan] Sleep Disorders Ctr Georgia, Atlanta, GA USA. [Mayleben, David] Community Res, Cincinnati, OH USA. [Stern, Theresa] Pfizer Inc, Ann Arbor, MI USA. [Pitman, Verne; Clark, David] Pfizer Inc, New London, CT USA. [Werth, John L.] Wyeth Res, Collegeville, PA USA.

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Study Objectives: Explore characteristics of nonrestorative sleep (NRS) in prospectively defined subgroups of individuals with NRS symptoms, investigate whether NRS can occur independently of difficulties initiating and maintaining sleep (DIS/DMS), and determine its effect on waking function. **Design:** Cross-sectional and longitudinal population-based study comparing patterns of daytime symptoms, and their persistence, in cohorts of subjects with NRS symptoms grouped according to presence or absence of DIS and DMS. **Setting:** 28 sleep centers in the US. **Participants:** Subjects reporting awakening unrestored or unrefreshed at least 3 times weekly over the previous 3 months were classified, based on self-reported sleep problems, to DIS (n = 138), DMS (n = 44), DIS+DMS (n = 125), and NRS-only (no DIS or DMS; n = 192) cohorts. Eighty healthy volunteers formed a control group. **Interventions:** None. **Measurements and Results:** Polysomnography confirmed DIS and/or DMS in 56/138 (41%), 18/44 (41%), and 37/125 (30%) subjects in DIS, DMS, and DIS+DMS cohorts, respectively; and absence of DIS or DMS in 115/192 (60%) NRS-only subjects and 52/80(65%) healthy volunteers. Multiple subject-reported endpoints including the Endicott Work Productivity Scale, Pittsburgh Insomnia Rating Scale, Restorative Sleep Questionnaire, and SF-36, showed that NRS-only subjects had significantly impaired daytime function relative to healthy volunteers, comparable to impairment affecting subjects with DIS and/or DMS. Symptoms persisted over 3 months. **Conclusions:** This study confirms that NRS can occur independently of other components of insomnia. Daytime symptoms were as severe in individuals with NRS-only as those whose NRS symptoms were combined with DIS or DMS.

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Surgery

Gao, X. H., D. Deeb, J. Hao, Y. B. Liu, A. S. Arbab, S. A. Dulchavsky and S. C. Gautam (2010). "Synthetic Triterpenoids Inhibit Growth, Induce Apoptosis and Suppress Pro-survival Akt, mTOR and NF- κ B Signaling Proteins in Colorectal Cancer Cells." [Anticancer Research](#) **30**(3): 785-792. [PDF Full-Text](#)

[Gao, Xiaohua; Deeb, Dorrah; Hao, Jiang; Liu, Yongbo; Arbab, Ali S.; Dulchavsky, Scott A.; Gautam, Subhash C.] Henry Ford Hlth Syst, Dept Surg, Detroit, MI USA.
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Lack of apoptotic cell death has been implicated in malignant transformation and resistance to anticancer therapies. The promotion of apoptosis in cancer cells could potentially lead to the regression and improved prognosis of refractory colorectal cancer. Synthetic triterpenoids have shown strong antitumorigenic activity towards diverse cancer cell types, but have not been investigated for colorectal cancer. In the present study, we tested the apoptosis-inducing activity of oleanane triterpenoid 2-cyano-3,12-diaxoleanal,9(11)-dien-28-oic acid (CDDO) and its C-28 methyl ester (CDDO-Me) and C-28 imidazole (CDDO-Im) derivatives in colorectal cancer cells lines. Cell growth/viability assay (MTS) demonstrated that colorectal cancer cells are highly sensitive to CDDO-Me at concentrations of 1.25 to 10 μ M. The primary mode of tumor cell destruction was apoptosis as demonstrated by the cleavage of PARP-1, activation of procaspases -3, -8, and -9 and mitochondrial depolarization. Induction of apoptosis by CDDO-Me was associated with the inhibition of pro-survival Akt, NF- κ B and mTOR signaling proteins and NF- κ B-regulated anti-apoptotic Bcl-2, Bcl-xL, Bad and survivin. These studies provide rationale for clinical evaluation of CDDO-Me for the treatment of advanced chemotherapy refractory colorectal cancer.

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Surgery

Khan, I., C. A. West, G. P. Sangster, M. Heldmann, L. Doucet and M. Olmedo (2010). "Multiple hereditary exostoses as a rare nonatherosclerotic etiology of chronic lower extremity ischemia." [Journal of Vascular Surgery](#) **51**(4): 1003-1005. [PDF Full-Text](#)

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Nonatherosclerotic etiologies of arterial insufficiency are uncommon but important causes of chronic lower extremity ischemia. We report a patient with multiple hereditary exostoses (MHE) presenting with lifestyle-limiting lower extremity claudication and popliteal artery occlusion secondary to a large osteochondroma. The presence of MHE with associated osteochondroma resulting in arterial occlusion is a rare condition. Management strategies for treating large osteochondromas adjacent to or with vessel involvement in asymptomatic patients remain undefined. (J Vasc Surg 2010; 51:1003-5.)

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Urology

Foster, H. E., P. M. Hanno, J. C. Nickel, C. K. Payne, R. D. Mayer, D. A. Burks, C. C. Yang, T. C. Chai, K. J. Kreder, K. M. Peters, E. S. Lukacz, M. P. FitzGerald, L. Y. Cen, J. R. Landis, K. J. Propert, W. Yang, J. W. Kusek and L. M. Nyberg (2010). "Effect of Amitriptyline on Symptoms in Treatment Naive Patients With Interstitial Cystitis/Painful Bladder Syndrome." [Journal of Urology](#) **183**(5): 1853-1858. [PDF Full-Text](#)

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Purpose: Amitriptyline is frequently used to treat patients with interstitial cystitis/painful bladder syndrome. The evidence to support this practice is derived mainly from a small, single site clinical trial and case reports. **Materials and Methods:** We conducted a multicenter, randomized, double-blind, placebo controlled clinical trial of amitriptyline in subjects with interstitial cystitis/painful bladder syndrome who were naive to therapy. Study participants in both treatment arms received a standardized education and behavioral modification program. The drug dose was increased during a 6-week period from 10 up to 75 mg once daily. The primary outcome was a patient reported global response assessment of symptom improvement evaluated after 12 weeks of treatment. **Results:** A total of 271 subjects were randomized and 231 (85%) provided a global response assessment at 12 weeks of followup. Study participants were primarily women (83%) and white (74%), with a median age of 38 years. In an intent to treat analysis (271) the rate of response of subjects reporting moderate or marked improvement from baseline in the amitriptyline and placebo groups was 55% and 45%, respectively ($p = 0.12$). Of the subgroup of subjects (207) who achieved a drug dose of at least 50 mg, a significantly higher response rate was observed in the amitriptyline group (66%) compared to placebo (47%) ($p = 0.01$). **Conclusions:** When all randomized subjects were considered, amitriptyline plus an education and behavioral modification program did not significantly improve symptoms in treatment naive patients with interstitial cystitis/painful bladder syndrome. However, amitriptyline may be beneficial in persons who can achieve a daily dose of 50 mg or greater, although this subgroup comparison was not specified in advance.

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Urology

Sarveswaran, S., C. E. Myers and J. Ghosh (2010). "MK591, a leukotriene biosynthesis inhibitor, induces apoptosis in prostate cancer cells: synergistic action with LY294002, an inhibitor of phosphatidylinositol 3'-kinase." Cancer Lett **291**(2): 167-76. [Article Request Form](#)

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MK591 is a synthetic compound which specifically inhibits the activity of 5-Lox and is currently under development for the treatment of asthma. We observed that human prostate cancer cells treated with MK591 undergo apoptosis within hours of treatment. Apoptosis involves severe morphological alteration, externalization of phosphatidyl-serine, cleavage of PARP, and degradation of chromatin-DNA. MK591 also induced rapid activation of the stress kinase, c-Jun N-terminal kinase (JNK), which plays an important role in the apoptosis process. The phosphatidylinositol 3'-kinase-Akt/protein kinase B (PI3K/Akt) axis is a well-known pro-survival pathway which prevents apoptosis through defined anti-apoptotic mechanisms in a variety of cancer cells. Interestingly, we observed that MK591 triggers apoptosis in prostate cancer cells without inhibition of PI3K-Akt, or ERK. Moreover, it was observed that MK591 and LY294002 (an inhibitor of PI3K) exert synergistic effect in inducing apoptosis in prostate cancer cells. Altogether, these findings indicate that 5-Lox inhibition-induced apoptosis in prostate cancer cells occurs without inhibition of PI3K-Akt, or ERK, and suggest for the existence of an Akt- and ERK-independent survival mechanism(s) in these cancer cells maintained via signals generated by metabolites of 5-Lox.

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