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You can access this page at http://www.henryford.com/body_nologin.cfm?id=46638.

Al-Mallah, M. H., I. M. Tleyjeh, A. A. Abdel-Latif, and W. D. Weaver. (2006). "Angiotensin-converting enzyme inhibitors in coronary artery disease and preserved left ventricular systolic function: a systematic review and meta-analysis of randomized controlled trials." *J Am Coll Cardiol* **47**(8): 1576-83. [PDF Full-Text](#)

OBJECTIVES: This study sought to assess the efficacy of angiotensin-converting enzyme inhibitors (ACEIs) in patients with coronary heart disease and preserved left ventricular (LV) function. BACKGROUND: The ACEIs have been shown to improve outcomes in patients with heart failure and myocardial infarction (MI). However, there is conflicting evidence concerning the benefits of ACEIs in patients with coronary artery disease (CAD) and preserved LV systolic function. METHODS: An extensive search was performed to identify randomized, placebo-controlled trials of ACEI use in patients with CAD and preserved LV systolic function. Of 61 potentially relevant articles screened, 6 trials met the inclusion criteria. They were reviewed to determine cardiovascular mortality, nonfatal MI, all-cause mortality, and revascularization rates. We performed random-effect model meta-analyses and quantified between-studies heterogeneity with I(2). RESULTS: There were 16,772 patients randomized to ACEI and 16,728 patients randomized to placebo. Use of ACEIs was associated with a decrease in cardiovascular mortality (relative risk [RR] 0.83, 95% confidence interval [CI] 0.72 to 0.96, p = 0.01), nonfatal MI (RR 0.84, 95% CI 0.75 to 0.94, p = 0.003), all-cause mortality (RR 0.87, 95% CI 0.81 to 0.94, p = 0.0003), and revascularization rates (RR 0.93, 95% CI 0.87 to 1.00, p = 0.04). There was no significant between-studies heterogeneity. Treatment of 100 patients for an average duration of 4.4 years prevents either of the adverse outcomes (one death, or one nonfatal myocardial infarction, or one cardiovascular death or one coronary revascularization procedure). CONCLUSIONS: The cumulative evidence provided by this meta-analysis shows a modest favorable effect of ACEIs on the outcome of patients with CAD and preserved LV systolic function.

Beal, A. C., S. C. Chou, R. H. Palmer, M. A. Testa, C. Newman, and S. Ezhuthachan. (2006). "The changing face of race: risk factors for neonatal hyperbilirubinemia." *Pediatrics* **117**(5): 1618-25. [PDF Full-Text](#)

OBJECTIVES: Race is a predictor of health outcomes and risk for some clinical conditions, for example, mother's race predicts risk for hyperbilirubinemia in newborns, with blacks at lowest risk. Little is known about the correlation of race as recorded in medical records with self-reported race. Also, use of maternal race to predict newborn risk for hyperbilirubinemia has not been tested for multiracial mothers and newborns. We sought to examine how maternal race documented in medical records correlates with self-reported race and to examine the correlation between mothers' and newborns' race in the context of risk for neonatal hyperbilirubinemia, focusing on multiracial mothers and newborns. DESIGN: A cohort study with 3021 newborns at > or =35 weeks gestation

discharged from normal nursery between January 2001 and October 2002 with a telephone survey of their mothers within 6 months of birth. SETTING: The study was conducted in the Neonatology Department of Henry Ford Hospital. PATIENTS: There were 1773 mothers (58%) with incorrect telephone numbers. Of 1248 mothers contacted, 866 (69%) completed the interview. OUTCOME MEASURES: We measured mother's race in hospital database and mother's reported race for herself, her newborn, and the father, allowing < or =5 responses for each. RESULTS: Of mothers documented in the medical record as white, 64% self-reported as white. Among mothers recorded as black, 70% self-reported as black. Mothers identified 93 newborns as > or =2 races with primary race matching both parents for 41%, father for 25%, mother for 23%, and neither parent for 11%. Of 70 newborns whose parents were not the same race, mothers identified 45 (64%) as > or =2 races. CONCLUSIONS: There is incomplete overlap between racial identification in medical records versus self-report. Given 1 choice, mothers of multiracial infants overselect black in their newborns' ancestry. Because black race is the lowest risk category for neonatal hyperbilirubinemia, this may lead to underestimating their risk.

Besarab, A. and S. Soman (2005). "Anemia management in chronic heart failure: lessons learnt from chronic kidney disease." Kidney Blood Press Res **28**(5-6): 363-71. **Full-Text Not Available** / [Click for Article Request Form](#)

The importance of anemia in chronic kidney disease (CKD) has become increasingly well recognized over recent years, as have the benefits of treating anemic CKD patients with recombinant human erythropoietin (rHuEPO, epoetin). As well as reducing the need for blood transfusions and the complications associated with renal failure in CKD patients, rHuEPO treatment decreases patient morbidity and mortality, particularly as a result of cardiovascular disease. The strong correlation between anemia, renal failure and cardiac failure is one that has received much attention recently, with each factor recognized to cause the other to worsen in a 'vicious cycle'. Recent studies have concentrated on the possible benefits of anemia treatment in patients with CHF. Currently available data suggest improvements in CHF symptoms, left ventricular ejection fraction (LVEF) and a reduction of hospitalizations associated with anemia correction through epoetin treatment. Available data from CKD patients suggest that anemia management should begin as early as possible, although the optimal target level for individual patients is as yet unclear. In addition to the currently available evidence, additional large, randomized, controlled studies are required to further define the morbidity/mortality benefits of epoetin treatment in CHF patients with anemia.

Billecke, C., S. Finniss, L. Tahash, C. Miller, T. Mikkelsen, N. P. Farrell, and O. Bogler. (2006). "Polynuclear platinum anticancer drugs are more potent than cisplatin and induce cell cycle arrest in glioma." Neuro-oncol. **Full-Text Not Available** / [Click for Article Request Form](#)

We have evaluated the efficacy of the multinuclear platinum chemotherapeutics BBR3464, BBR3571, and BBR3610 against glioma cells in culture and animal models and investigated their mechanism of action at the cellular level. In a clonogenic assay, BBR3610, the most potent compound, had an IC90 dose (achieving 90% colony formation inhibition) that was 250 times lower than that of cisplatin for both LN2308 and LN443 glioma cells. In subcutaneous xenografts of U87MG glioma cells, BBR3610 approximately doubled the time it took for a tumor to reach a predetermined size and significantly extended survival when these cells were implanted intracranially. Analysis of apoptosis and cell cycle distribution showed that BBR compounds induced G2/M arrest in the absence of cell death, while cisplatin predominantly induced apoptosis. Interestingly, the BBR compounds and cisplatin both induced extracellular signal-regulated kinase 1/2 phosphorylation, and inhibition of this pathway at the level of MEK antagonized the induction of G2/M arrest or apoptosis, respectively. Analysis of Chk1 and Chk2 status did not show any differential effects of the drugs, and it is thus unlikely to underlie the difference in response. Similarly, the drugs did not differentially modulate survivin levels, and knockdown of survivin did not convert the response to BBR3610 to apoptosis. Together, these findings support continued development of BBR3610 for clinical use against glioma and provide a framework for future investigation of mechanism of action.

Brawner, C. A., J. K. Ehrman, and S. J. Keteyian. (2006). "Impact of Obesity on the Cardiorespiratory Response to Exercise: 939: 8:45 AM - 9:00 AM." Med Sci Sports Exerc **38**(5 Suppl): S85. [PDF Full-Text](#)

Cerghet, M., R. P. Skoff, D. Bessert, Z. Zhang, C. Mullins, and M. S. Ghandour. (2006). "Proliferation and death of oligodendrocytes and myelin proteins are differentially regulated in male and female rodents." *J Neurosci* **26**(5): 1439-47. [PDF Full-Text](#)

Sexual dimorphism of neurons and astrocytes has been demonstrated in different centers of the brain, but sexual dimorphism of oligodendrocytes and myelin has not been examined. We show, using immunocytochemistry and in situ hybridization, that the density of oligodendrocytes in corpus callosum, fornix, and spinal cord is 20-40% greater in males compared with females. These differences are present in young and aged rodents and are independent of strain and species. Proteolipid protein and carbonic anhydrase-II transcripts, measured by real-time PCR, are approximately two to three times greater in males. Myelin basic protein and 2', 3'-cyclic nucleotide 3'-phosphodiesterase, measured by Western blots, are 20-160% greater in males compared with females. Surprisingly, both generation of new glia and apoptosis of glia, including oligodendrocytes, are approximately two times greater in female corpus callosum. These results indicate that the lifespan of oligodendrocytes is shorter in females than in males. Castration of males produces a female phenotype characterized by fewer oligodendrocytes and increased generation of new glia. These findings indicate that exogenous androgens differentially affect the lifespan of male and female oligodendrocytes, and they can override the endogenous production of neurosteroids. The data imply that turnover of myelin is greater in females than in males. Mu-calpain, a protease upregulated in degeneration of myelin, is dramatically increased at both transcriptional and translational levels in females compared with males. These morphological, molecular, and biochemical data show surprisingly large differences in turnover of oligodendrocytes and myelin between sexes. We discuss the potential significance of these differences to multiple sclerosis, a sexually dimorphic disease, whose progression is altered by exogenous hormones.

Cooper, G. S., C. C. Johnson, L. Lamerato, L. M. Poisson, L. Schultz, J. Simpkins, K. Wells, M. U. Yood, G. Chase, S. D. Nathanson, and J. E. Lafata. (2006). "Use of Guideline Recommended Follow-Up Care in Cancer Survivors: Routine or Diagnostic Indications?" *Med Care* **44**(6): 590-594. [PDF Full-Text](#)

BACKGROUND:: After potentially curative cancer treatment, patients may receive procedures for routine monitoring for recurrence or for evaluation of symptoms or signs. **OBJECTIVE::** We sought to characterize surveillance care guideline-recommended and other procedures performed in cancer survivors according to routine versus diagnostic indications. **METHODS::** This was a retrospective cohort study of paper and electronic medical records between 1990 and 2000 from a large midwestern U.S. integrated health care delivery system of 500 patients who received curative treatment of breast, colorectal, endometrial, lung, or prostate cancer. Our measures were the indications for potential surveillance procedures as recommended by clinical practice guidelines or otherwise. **RESULTS::** Among 14,670 procedures of interest received, 82.0% were performed for routine surveillance, whereas 10.6% were performed for diagnostic indications and 7.3% had indeterminate indications. Office visits most were often delivered for routine indications (91.6%), followed by guideline recommended tests for local recurrence (range 74.1-98.4%, depending on the specific test and cancer). In general, tests that were not recommended in established guidelines were for the purposes of detection of metastatic recurrence and were less often delivered for routine indications (overall frequency 59.2%, $P < 0.0001$ compared with recommended testing). **CONCLUSION::** Office visits and testing for local recurrence of cancer generally are performed for routine surveillance, regardless of recommendation by practice guidelines. Because procedures not recommended by practice guidelines were more often for diagnostic purposes, classification of patients as undergoing intensive surveillance may be misleading and may require record review to confirm.

Deeb, D., X. Gao, H. Jiang, G. Divine, S. A. Dulchavsky, and S. C. Gautam. (2006). "Vaccination with leukemia-loaded dendritic cells eradicates residual disease and prevent relapse." *J Exp Ther Oncol* **5**(3): 183-93. **Full-Text Not Available** / [Click for Article Request Form](#)

We have previously demonstrated that TNF-alpha gene therapy with myeloid progenitor cells inhibits the progression of 32Dp210 myeloid leukemia in mice. Because TNF-alpha has been shown to induce the activation and maturation of dendritic cells (DCs), we investigated the efficacy of DC-based leukemia vaccine for eradication of residual disease when administered following cytoreductive therapy. Immunization with DC cells loaded with 32Dp210 myeloid leukemia cells (32Dp210 vaccine) was far more effective in preventing the development of leukemia compared to immunization with irradiated leukemia cells alone. The resistance to leukemia could be

adoptively transferred to naive mice with the spleen cells of mice immunized with DC-32Dp210 vaccine, and splenic cells responsible for adoptive transfer of resistance were identified as CD90 + T lymphocytes. Development of immunity in vaccinated mice was associated with the generation of leukemia specific cytotoxic T lymphocytes (CTLs) and secretion of cytokines TNF-alpha and IFN-gamma. Further, immunization with DC-32Dp210 vaccine following cytoreductive therapy with Cytoxan was effective in eradicating residual disease in approximately 50 percent of the animals. However, eradication of residual disease was significantly improved (approximately 74%) when animals were treated with DC-32Dp210 vaccine in which DCs were activated with TNF-alpha prior to loading of 32Dp210 leukemia cells. Cured mice were in molecular remission since Bcr/Abl oncogene could not be amplified from the DNA isolated from the marrow, spleen, or liver of cured mice. Taken together, these data demonstrate the efficacy of DC-based leukemia vaccine for eradication of residual disease and prevention of relapse.

Divi, V. and M. S. Benninger (2006). "Diagnosis and management of laryngopharyngeal reflux disease." *Curr Opin Otolaryngol Head Neck Surg* **14**(3): 124-7. [PDF Full-Text](#)

PURPOSE OF REVIEW: The recent findings and up-to-date practice guidelines for diagnosing, evaluating, and treating gastro-esophageal reflux disease are discussed. **RECENT FINDINGS:** The patient complaints for reflux disease are crucial in diagnosis. Although physical examination findings may correlate with laryngopharyngeal reflux, these findings may not improve after an adequate course of treatment. Behavioral modifications are a critical part of improving reflux; however, weight loss has not been shown to improve laryngopharyngeal reflux disease. Patients who used proton-pump inhibitors and histamine blockers were shown to have increased risk of developing *Clostridium difficile* infections. Laryngopharyngeal reflux has been shown to be a better predictor of Barrett's esophagus than gastroesophageal reflux, although specific screening recommendations have not been determined. **SUMMARY:** Current studies in laryngopharyngeal reflux demonstrate that improvements in physical examination findings are not a reliable way of determining patient improvement. An empiric trial of therapy is the best diagnostic test for laryngopharyngeal reflux. Future studies will examine the role of transnasal esophagoscopy in the screening of the laryngopharyngeal reflux patient for Barrett's esophagus.

Guana, H. (2006). "Time delay study of a CT simulator in respiratory gated CT scanning." *Med Phys* **33**(4): 815-9. **Full-Text Not Available / [Click for Article Request Form](#)**

In respiratory-gated radiotherapy (RGRT), if the time delay in a computed tomography (CT) simulator and that in a linear accelerator (Linac) are different, the simulation and the treatment cannot be synchronized. In this study, we presented a technique to measure the time delay of the AcQSim CT simulator (Philips Medical Systems, Cleveland, OH) using Varian's Real-Time Positioning Management (RPM) system (Varian Medical Systems, Palo Alto, CA). A respiratory gating platform (REF 91150, Standard Imaging, Inc., Middleton, MI) was first set at the position of amplitude maximum (phase 0). Then a ball of 1.3 cm diameter was put on the platform and set at the CT laser. A single axial scan was acquired across the center of the ball without motion. Then the motion was turned on and single axial scans gated at different phases were acquired with a very narrow gating window. The time between the phase giving a good estimate of the ball and phase 0 is the overall delay time. We found that for AcQSim CT, the overall delay for a single axial scan (with 1 s scan time) is 1.75 s. For multiple axial scans, the overall delay is 1.75 s for the first scan and 0.75 s for the subsequent ones. This demonstrated that the CT mechanical startup delay is 1 s. After the first axial scan, the overall delay per scan is less because CT gantry continuously spins and no mechanical delay exists. We call the overall delay without mechanical part the scanning delay, which basically equals half the scan time (0.5 s for 1 s scan time) plus the gating pulse triggering delay (250 ms). The delays were also verified using metal balls of 1.5 mm diameter set at the amplitude minimum (phase 180, initially). We note that it is the scanning delay rather than the triggering delay that should be compensated when doing motion-synchronized radiotherapy. The current interface between the RPM system and the AcQSim CT does not compensate for this scanning delay.

Guo, M., R. J. Roman, J. D. Fenstermacher, S. L. Brown, J. R. Falck, A. S. Arbab, P. A. Edwards, and A. G. Scicli. (2006). "9L gliosarcoma cell proliferation and tumor growth in rats are suppressed by N-hydroxy-N'-(4-butyl-2-methylphenol) formamidine (HET0016), a selective inhibitor of CYP4A." *J Pharmacol Exp Ther* **317**(1): 97-108. [PDF Full-Text](#)

The present study examined the effects of N-hydroxy-N'-(4-butyl-2 methylphenyl) formamidine (HET0016), a selective inhibitor of the formation of 20-hydroxyeicosatrienoic acid (20-HETE) on the growth of 9L rat gliosarcoma cells in vitro and in vivo. After 48 h of incubation, HET0016 reduced the proliferation of 9L in vitro

by 55%, and this was associated with a fall in p42/p44 mitogen-activated protein kinase and stress-activated protein kinase/c-Jun NH(2)-terminal kinase phosphorylation and increased apoptosis. HET0016 inhibited epidermal growth factor (EGF) and platelet-derived growth factor (PDGF)-induced proliferation and diminished phosphorylation of PDGF receptors. A stable 20-HETE analog increased 9L cell proliferation. In vivo, chronic administration of HET0016 (10 mg/kg/day i.p.) for 2 weeks reduced the volume of 9L tumors by 80%. This was accompanied by a 4-fold reduction in the mitotic index, a 3- to 4-fold increase in the apoptotic index, and an approximately 50% decrease in vascularization in the tumor. HET0016 treatment increased mean survival time of the animals from 17 to 22 days. Liquid chromatography/mass spectrometry experiments indicated that neither 9L cells grown in vitro nor 9L tumors removed produce 20-HETE when incubated with arachidonic acid. The normal surrounding brain tissue, however, avidly makes 20-HETE, and this activity is selectively inhibited by HET0016. These results suggest that HET0016 may be the prototype of a class of antigrowth compounds that may be efficacious for treating malignant brain tumors. In vivo, it may act in part by inhibiting the formation of 20-HETE by the surrounding tissue. However, the antiproliferative effects of HET0016 on 9L cells in vitro seem unrelated to its ability to inhibit the formation of 20-HETE.

Herrera, M., N. J. Hong, and J. L. Garvin. (2006). "Aquaporin-1 Transports NO Across Cell Membranes." *Hypertension*. [PDF Full-Text](#)

NO plays a role in the regulation of blood pressure through its effects on renal, cardiovascular, and central nervous system function. It is generally thought to freely diffuse through cell membranes without need for a specific transporter. The water channel aquaporin-1 transports low molecular weight gases in addition to water and is expressed in cells that produce or are the targets of NO. Consequently, we tested the hypothesis that aquaporin-1 transports NO. In cells expressing aquaporin-1, NO permeability correlated with water permeability. NO transport was reduced by 71% by HgCl₂, an inhibitor of aquaporin-1. Transport of NO by aquaporin-1 saturated at 3 micromol/L NO and displayed a K_{1/2} (the concentration of NO that produces half of the maximum transport rate) of 0.54 micromol/L. Reconstitution of purified aquaporin-1 into lipid vesicles increased NO influx by 316%. In endothelial cells, lowering aquaporin-1 expression with a small interfering RNA (siRNA) blunted aquaporin-1 expression by 54% and NO release by 44%. We conclude that NO transport by aquaporin-1 may allow cells to control intracellular NO levels and effects. NO transport by aquaporin-1 may play a role in central nervous system, vascular and renal function, and consequently blood pressure. Disruption of NO transport by aquaporin-1 offers an alternate cause for diseases currently explained by inadequate NO bioavailability.

Herrera, M., P. A. Ortiz, and J. L. Garvin. (2006). "Regulation of thick ascending limb transport: role of nitric oxide." *Am J Physiol Renal Physiol* **290**(6): F1279-84. [PDF Full-Text](#)

Nitric oxide (NO) plays a role in many physiological and pathophysiological processes. In the kidney, NO reduces renal vascular resistance, increases glomerular filtration rate, alters renin release, and inhibits transport along the nephron. The thick ascending limb is responsible for absorbing 20-30% of the filtered load of NaCl, much of the bicarbonate that escapes the proximal nephron, and a significant fraction of the divalent cations reclaimed from the forming urine. Additionally, this nephron segment plays a role in K⁺ homeostasis. This article will review recent advances in our understanding of the role NO plays in regulating the transport processes of the thick ascending limb. NO has been shown to inhibit NaCl absorption primarily by reducing Na⁺-K⁺-2Cl⁻ cotransport activity. NO also inhibits bicarbonate absorption by reducing Na⁺/H⁺ exchange activity. It has also been reported to enhance luminal K⁺ channel activity and thus is likely to alter K⁺ secretion. The source of NO may be vascular structures such as the afferent arteriole or vasa recta, or the thick ascending limb itself. NO is produced by NO synthase 3 in this segment, and several factors that regulate its activity both acutely and chronically have recently been identified. Although the effects of NO on thick ascending limb transport have received a great deal of attention recently, its effects on divalent ion absorption and many other issues remain unexplored.

Jiang, F., Z. Zhang, S. Kalkanis, M. Katakowski, A. M. Robin, X. Zhang, A. Gotlib, I. Chelst, T. Mikkelsen, and M. Chopp. (2005). "A quantitative model of tumor-induced angiogenesis in the nude mouse." *Neurosurgery* **57**(2): 320-4. [PDF Full-Text](#)

OBJECTIVE: Novel animal models allowing for the quantification of tumor-induced angiogenesis and cell migration may offer significant insight into the characterization and multidisciplinary treatment of brain tumors. In this study, we seek to establish such a model in tumor-bearing brain, allowing for a clear demarcation of primary and satellite tumor tissue in conjunction with precise quantification of cerebral microvasculature. METHODS: We

used green fluorescent protein-transfected 9L-gliosarcoma cells stereotactically injected into the brain parenchyma of nude mice perfused with tetramethylrhodamine-dextran immediately before they were killed. New three-dimensional analytical software developed in our laboratory provided a quantitative analysis of laser-scanning confocal microscopy images of dextran-labeled cerebral microvessels. RESULTS: Our data confirm significant angiogenesis in tumor and brain adjacent to tumor. CONCLUSION: Because these highly infiltrative malignant brain tumors interdigitate with normal brain parenchyma through finger-like projections at the periphery of the solid tumor boundary, therapeutic options targeting tumor blood flow--combined with novel three-dimensional imaging to localize and track such interventions--may offer new hope for glioma management. To our knowledge, this system represents the first animal brain tumor model allowing for the precise colocalization and quantification of angiogenesis and tumor cell invasion, which may play an important role in the development of future therapy for brain tumors.

Kaul, S. and M. Menon (2006). "Robotic radical prostatectomy: evolution from conventional to VIP." World J Urol. **Full-Text Not Available / [Click for Article Request Form](#)**

Following the popularization of Vattikuti Institute Prostatectomy technique of robotic radical prostatectomy (RARP) by Menon et al., RARP has been gaining steady acceptance as a preferred alternative to both open and laparoscopic radical prostatectomy (LRP). Up until now, radical retropubic prostatectomy has been considered the gold standard for treatment of organ confined prostate cancer. Despite significant improvements in intraoperative blood loss and functional outcomes, driven primarily by the description of anatomical radical prostatectomy by Walsh, the perioperative morbidity, analgesic requirement, and recovery times have remained disadvantages of the open approach. LRP has been unable to gain widespread acceptance because of technical difficulty and a steep learning curve. The da Vinci assisted approach incorporates the advantages of minimally invasive approach while improving upon the results of the open approach. This paper traces the evolution of RARP and describes technical modifications incorporated at the Vattikuti Urology Institute including operative data, complications, and functional outcomes.

Kaul, S. A., J. O. Peabody, N. Shah, D. Neal, and M. Menon. (2006). "Establishing a Robotic Prostatectomy Programme: the Impact of Mentoring Using a Structured Approach." BJU Int **97**(6): 1143-1144. [PDF Full-Text](#)

Keteyian, S. J. (2006). "886." Med Sci Sports Exerc **38**(5 Suppl): S73. [PDF Full-Text](#)

Keteyian, S. J. (2006). "Exercise rehabilitation in chronic heart failure." Coron Artery Dis **17**(3): 233-7. [PDF Full-Text](#)

The past 15 years of research involving patients with heart failure have provided a lot of new information regarding how exercise training lessens the exercise intolerance that is characteristic of these patients. Despite these new understandings, the prescription of regular exercise and rehabilitation in eligible patients is not embraced by all practitioners. Such reluctance may be due, in part, to concerns about either the safety of the treatment or the absence of multisite, randomized, controlled trial data that evaluates clinical end-points. This paper focuses on how exercise capacity is improved through training in patients with heart failure and suggests future considerations with respect to the study and application of this novel therapy.

Keteyian, S. J., C. A. Brawner, and J. K. Ehrman. (2006). "Validating Multiple Sites for Exercise Testing in Clinical Trials: Role of an Exercise Core Laboratory: 936: 8:00 AM - 8:15 AM." Med Sci Sports Exerc **38**(5 Suppl): S84. [PDF Full-Text](#)

Kontos, A. P., H. A. Kerr, F. Malick, D. P. Fivenson, H. W. Lim, and H. K. Wong. (2006). "308-nm Excimer laser for the treatment of lymphomatoid papulosis and stage IA mycosis fungoides." Photodermatol Photoimmunol Photomed **22**(3): 168-71. **Full-Text Not Available / [Click for Article Request Form](#)**

Kullavanijaya, P. and H. W. Lim (2005). "Photoprotection." *J Am Acad Dermatol* **52**(6): 937-58; quiz 959-62. [PDF Full-Text](#)

Many agents affect the transmission of ultraviolet light to human skin. These include naturally occurring photoprotective agents (ozone, pollutants, clouds, and fog), naturally occurring biologic agents (epidermal chromophores), physical photoprotective agents (clothing, hats, make-ups, sunglasses, and window glass), and ultraviolet light filters (sunscreen ingredients and sunless tanning agents). In addition, there are agents that can modulate the effects of ultraviolet light on the skin (antioxidants and others). All of the above are reviewed in this article. LEARNING OBJECTIVE: At the conclusion of this learning activity, participants should be able to provide an overview of all aspects of photoprotection.

Lafata, J. E., L. Schultz, J. Simpkins, K. A. Chan, J. R. Horn, S. Kaatz, C. Long, R. Platt, M. A. Raebel, D. H. Smith, H. Xi, and M. U. Yood. (2006). "Potential Drug-Drug Interactions in the Outpatient Setting." *Med Care* **44**(6): 534-541. [PDF Full-Text](#)

BACKGROUND:: Although medication safety research has tended to focus on inpatients, the safety of drug use among outpatients is also a concern. OBJECTIVE:: We estimate the frequency of potentially interacting concomitant medication dispensing among outpatients. RESEARCH DESIGN:: We report the number and percent of patients annually dispensed an object drug of interest (ie, warfarin, digoxin, cyclosporine, or lovastatin/simvastatin) with a potentially interacting drug among a random sample of insured adults receiving care from 10 integrated delivery systems. We use 2 definitions of concomitant dispensing: medications dispensed: 1) during the time period for which the patient had the other medication available ('days supply') and 2) on the same day. We also estimate the number of insured U.S. population codispensed these medication pairs. RESULTS:: Among patients dispensed a drug of interest, between 17.8% (95% confidence interval [CI] = 17.1-18.6%) and 28.0% (95% CI = 24.0-32.1%) were concomitantly dispensed a potentially interacting drug using the "days supply" definition, and between 7.1% (95% CI = 6.6-7.7%) and 17.7% (95% CI = 14.4-21.1%) using the "same day" definition. Extrapolating to the insured U.S. population, between 1.29 (95% CI = 1.25-1.33; same day) and 2.67 (95% CI = 2.62-2.72; days supply) million insured adults are dispensed 1 of these 4 potentially interacting pairs. CONCLUSIONS:: We found evidence of potentially interacting concomitant medication dispensing among outpatients. An opportunity exists to better understand how such dispensing translates into adverse events and ultimately to improved medication safety.

Li, S., D. Liu, G. Yin, P. Zhuang, and J. Geng. (2006). "Real-time 3D-surface-guided head refixation useful for fractionated stereotactic radiotherapy." *Med Phys* **33**(2): 492-503. **Full-Text Not Available** / [Click for Article Request Form](#)

Accurate and precise head refixation in fractionated stereotactic radiotherapy has been achieved through alignment of real-time 3D-surface images with a reference surface image. The reference surface image is either a 3D optical surface image taken at simulation with the desired treatment position, or a CT/MRI-surface rendering in the treatment plan with corrections for patient motion during CT/MRI scans and partial volume effects. The real-time 3D surface images are rapidly captured by using a 3D video camera mounted on the ceiling of the treatment vault. Any facial expression such as mouth opening that affects surface shape and location can be avoided using a new facial monitoring technique. The image artifacts on the real-time surface can generally be removed by setting a threshold of jumps at the neighboring points while preserving detailed features of the surface of interest. Such a real-time surface image, registered in the treatment machine coordinate system, provides a reliable representation of the patient head position during the treatment. A fast automatic alignment between the real-time surface and the reference surface using a modified iterative-closest-point method leads to an efficient and robust surface-guided target refixation. Experimental and clinical results demonstrate the excellent efficacy of <2 min set-up time, the desired accuracy and precision of <1 mm in isocenter shifts, and <1 degree in rotation.

Li, X. C., D. J. Campbell, M. Ohishi, S. Yuan, and J. L. Zhuo. (2006). "AT1 receptor-activated signaling mediates angiotensin IV-induced renal cortical vasoconstriction in rats." *Am J Physiol Renal Physiol* **290**(5): F1024-33. [PDF Full-Text](#)

Angiotensin IV (ANG IV), an active ANG II fragment, has been shown to induce systemic and renal cortical effects by binding to ANG IV (AT(4)) receptors and activating unique signaling transductions unrelated to classical type 1 (AT(1)) or type 2 (AT(2)) receptors. We tested whether ANG IV exerts systemic and renal cortical

effects on blood pressure, renal microvascular smooth muscle cells (VSMCs), and glomerular mesangial cells (MC) and, if so, whether AT(1) receptor-activated signaling is involved. In anesthetized rats, systemic infusion of ANG II, ANG III, or ANG IV (0.01, 0.1, and 1.0 nmol.kg(-1).min(-1) iv) caused dose-dependent increases in mean arterial pressure (MAP) and decreases in renal cortical blood flow (CBF; $P < 0.01$). ANG II also induced dose-dependent reductions in renal medullary blood flow ($P < 0.01$), whereas ANG IV did not. ANG IV-induced pressor and renal cortical vasoconstriction were completely abolished by AT(1) receptor blockade with losartan (5 mg/kg iv; $P < 0.05$). When ANG IV (1 nmol.kg(-1).min(-1)) was infused directly in the renal artery, CBF was reduced by $>30\%$, and the response was also blocked by losartan ($P < 0.01$). In the renal cortex, unlabeled ANG IV displaced (125)I-labeled [Sar(1),Ile(8)]ANG II binding, whereas unlabeled ANG II (10 microM) inhibited (125)I-labeled Nle(1)-ANG IV (AT(4)) binding in a concentration-dependent manner ($P < 0.01$). In freshly isolated renal VSMCs, ANG IV (100 nM) increased intracellular Ca(2+) concentration, and the effect was blocked by losartan and U-73122, a selective inhibitor of phospholipase C/inositol trisphosphate/Ca(2+) signaling (1 microM). In cultured rat MCs, ANG IV (10 nM) induced mitogen-activated protein kinase extracellular/signal-regulated kinase 1/2 phosphorylation via AT(1) receptor- and phospholipase C-activated signaling. These results suggest that, at nanomolar concentrations, ANG IV can increase MAP and induce renal cortical effects by interacting with AT(1) receptor-activated signaling.

Li, X. C., O. A. Carretero, and J. L. Zhuo. (2006). "Cross-talk between angiotensin II and glucagon receptor signaling mediates phosphorylation of mitogen-activated protein kinases ERK 1/2 in rat glomerular mesangial cells." *Biochem Pharmacol* **71**(12): 1711-9. **Full-Text Not Available / [Click for Article Request Form](#)**

We have recently shown that the pancreatic hormone glucagon-induced phosphorylation of mitogen-activated protein (MAP) kinase ERK 1/2 as well as growth and proliferation of rat glomerular mesangial cells (MCs) via activation of cAMP-dependent protein kinase A (PKA)-and phospholipase C (PLC)/Ca(2+)-mediated signaling pathways. Since circulating glucagon and tissue angiotensin II (Ang II) levels are inappropriately elevated in type 2 diabetes, we tested the hypothesis that glucagon induces phosphorylation of ERK 1/2 in MCs by interacting with Ang II receptor signaling. Stimulation of MCs by glucagon (10nM) induced a marked increase in intracellular [Ca(2+)](i) that was abolished by [Des-His(1), Glu(9)]-glucagon (1muM), a selective glucagon receptor antagonist. Both glucagon and Ang II-induced ERK 1/2 phosphorylation (glucagon: 214+/-14%; Ang II: 174+/-16%; $p < 0.001$ versus control), and these responses were inhibited by the AT(1) receptor blocker losartan (glucagon+losartan: 77+/-14%; Ang II+losartan: 84+/-18%; $p < 0.01$ versus glucagon or Ang II) and the AT(2) receptor blocker PD 123319 (glucagon+PD: 78+/-7%; Ang II+PD: 87+/-7%; $p < 0.01$ versus glucagon or Ang II). Inhibition of cAMP-dependent PKA with H89 (1muM) or PLC with U73122 (1muM) also markedly attenuated the phosphorylation of ERK 1/2 induced by glucagon (glucagon+U73122: 109+/-15%; glucagon+H89: 113+/-16%; $p < 0.01$ versus glucagon) or Ang II (Ang II+U73122: 111+/-13%; Ang II+H89: 86+/-10%; $p < 0.01$ versus Ang II). Wortmannin (1muM), a selective PI 3-kinase inhibitor, also blocked glucagon- or Ang II-induced ERK 1/2 phosphorylation. These results suggest that AT(1) receptor-activated cAMP-dependent PKA, PLC and PI 3-kinase signaling is involved in glucagon-induced MAP kinase ERK 1/2 phosphorylation in MCs. The inhibitory effect of PD 123319 on glucagon-induced ERK 1/2 phosphorylation further suggests that AT(2) receptors also play a similar role in this response.

Lim, H. W., B. A. Gilchrest, K. D. Cooper, H. A. Bischoff-Ferrari, D. S. Rigel, W. H. Cyr, S. Miller, V. A. DeLeo, T. K. Lee, C. A. Demko, M. A. Weinstock, A. Young, L. S. Edwards, T. M. Johnson, and S. P. Stone. (2005). "Sunlight, tanning booths, and vitamin D." *J Am Acad Dermatol* **52**(5): 868-76. **[PDF Full-Text](#)**

Mahmood, A., D. Lu, C. Qu, A. Goussev, and M. Chopp. (2005). "Human marrow stromal cell treatment provides long-lasting benefit after traumatic brain injury in rats." *Neurosurgery* **57**(5): 1026-31; discussion 1026-31. **[PDF Full-Text](#)**

OBJECTIVE: This study was designed to investigate the effects of human bone marrow stromal cell (hMSC) administration in rats for 3 months after traumatic brain injury (TBI). **METHODS:** Adult male Wistar rats (n = 60) were injured with controlled cortical impact and divided into four groups. The three treatment groups (n = 10 each) were injected with 2 x 10, 4 x 10, and 8 x 10 hMSCs, respectively, intravenously, whereas the control group (n = 30) received phosphate-buffered saline. All injections were performed 1 day after injury into the tail

veins of rats. Neurological functional evaluation of animals was performed before and after injury by use of Neurological Severity Scores. Animals were sacrificed 3 months after TBI, and brain sections were stained by immunohistochemistry. **RESULTS:** Statistically significant improvement in functional outcome was observed in all three treatment groups compared with control values ($P < 0.05$). This benefit was visible 14 days after TBI and persisted until 3 months (end of trial). There was no difference in functional outcome among the three treatment groups. Histological analysis showed that hMSCs were present in the lesion boundary zone at 3 months with all three doses tested. **CONCLUSION:** hMSCs injected in rats after TBI survive until 3 months and provide long-lasting functional benefit. Functional improvement may be attributed to stimulation of endogenous neurorestorative functions such as neurogenesis and synaptogenesis.

Maltsev, V. A. and A. I. Undrovinas (2006). "A multi-modal composition of the late Na^+ current in human ventricular cardiomyocytes." *Cardiovasc Res* **69**(1): 116-27. [PDF Full-Text](#)

OBJECTIVE: We reported an ultraslow late Na^+ current (INaL) in ventricular cardiomyocytes of human hearts. INaL has been implicated in regulation of action potential duration in normal hearts and repolarization abnormalities in failing hearts. We have also identified sodium channel (NaCh) gating modes including bursts (BM) and late scattered openings (LSM) that together comprise INaL ; however, the contribution of these gating modes to Na^+ current (INa) remains unknown. In the present study, the late NaCh activity was recorded, analyzed, and modeled for heterologously expressed NaCh , Nav1.5 , and for the native NaCh of ventricular mid-myocardial cardiomyocytes from normal and failing hearts. **METHODS AND RESULTS:** We found that LSM gating was significantly slower in failing compared to normal myocytes and Nav1.5 ($\tau = 474 \pm 10$ vs. 299 ± 9 , and 229 ± 12 ms, $m \pm \text{SEM}$; $P < 0.05$, $n = 5-6$). Total burst length of BM decreased with depolarization and was larger in failing compared to normal myocytes and Nav1.5 . A complete INa decay was then numerically approximated as composed of NaCh populations operating in three gating modes described by separate Markov kinetic schemes: transient mode (TM), LSM, and BM. The populations of NaCh operating in each gating mode were estimated as 79.8% for TM, 20% for LSM, and 0.2% for BM, yielding an apparent four-exponential INa decay at -30 mV (maximum INa) (τ approximately 0.4, 4, 50, and 500 ms). Whole-cell recordings confirmed the existence of all four predicted components. The model also predicted voltage and temperature dependence of INaL as well as INaL increase and slower decay in failing hearts and acceleration by amiodarone. **CONCLUSIONS:** The early phase of Na^+ current decay (< 40 ms) involves all three NaCh gating modes, the intermediate phase (from 40 to 300 ms) is produced by BM+LSM, although the contribution of BM decreases with depolarization, and ultra-late decay (> 300 ms) is determined solely by LSM. The concept of multi-mode composition for INaL provides a new rationale for INaL modulation by factors such as voltage, temperature, pharmacological agents, and pathological conditions.

McFarlin, K., A. E. Sargsyan, S. Melton, D. R. Hamilton, and S. A. Dulchavsky. (2006). "A surgeon's guide to the universe." *Surgery* **139**(5): 587-90. [PDF Full-Text](#)

Monaghan, K. G. and D. L. Van Dyke. (2006). Laboratory testing for Prader-Willi syndrome. *Management of Prader-Willi Syndrome*. M. G. Butler, Editor. New York, Springer-Verlag. **Full-Text Not Available / [Click for Chapter Request Form](#)**

Nathanson, S. D., R. Slater, D. Debruyne, A. Kapke, and M. Linden. (2006). "Her-2/neu expression in primary breast cancer with sentinel lymph node metastasis." *Ann Surg Oncol* **13**(2): 205-13. [PDF Full-Text](#)

BACKGROUND: Amplification of the protein product of the HER-2/neu oncogene in primary breast cancer specimens is associated with an adverse prognosis. We hypothesized that overexpression of HER-2/neu would predict metastases to the sentinel lymph nodes (SLNs). **METHODS:** A retrospective review of a prospective nonrandomized evaluation of 1055 clinically node-negative breast cancer patients undergoing 1063 SLN biopsies was performed. HER-2/neu analysis was performed by immunohistochemistry and, in selected cases, by fluorescence in situ hybridization. Clinical, demographic, surgical, radiological, and pathologic data were analyzed by using generalized estimating equations logistic regression models. **RESULTS:** Two hundred thirty-two (23.6%) of 985 operations in which the SLN was found at operation resulted in positive nodes. In a multivariate analysis, size ($P < .0001$) and HER-2/neu overexpression ($P = .026$) were independent predictors of SLN metastasis. **CONCLUSIONS:** Size is a known predictor of SLN metastasis in the modern SLN era, as it was in the pre-SLN

eras. HER-2/neu was found to be significantly predictive of SLN metastasis in our study. We anticipate a future when even the relatively minor procedure of SLN biopsy might be avoided with the predictive information gained from studying the pathology and molecular markers of primary breast cancers.

Nowak, R., C. Emerman, J. P. Hanrahan, M. V. Parsey, N. A. Hanania, R. Claus, K. Schaefer, and R. A. Baumgartner. (2006). "A comparison of levalbuterol with racemic albuterol in the treatment of acute severe asthma exacerbations in adults." *Am J Emerg Med* **24**(3): 259-67.

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This multicenter, randomized, double-blind trial compared nebulized levalbuterol (Lev) and racemic albuterol (Rac) in the treatment of acute asthma. **METHODS:** Adults with acute asthma exacerbations (FEV(1) 20%-55% predicted) received prednisone and either Lev (1.25 mg, n = 315) or Rac (2.5 mg, n = 312). Nebulized treatments were administered every 20 minutes in the first hour, then every 40 minutes for 3 additional doses, then as necessary for up to 24 hours. The primary end point was time to meet discharge criteria. Secondary end points included changes in lung function and hospitalization rates. A subset of 160 patients had plasma (S)-albuterol concentrations determined at study entry. **RESULTS:** Time to meet discharge criteria did not differ between the 2 treatments. FEV(1) improvement was greater following Lev compared with Rac, both after dose 1 and cumulatively over the entire treatment period (dose 1 in intent to treat [ITT] group: Lev 0.50 +/- 0.43 L, Rac 0.43 +/- 0.37 L; P = .02), particularly among the 60% of patients not on recent steroid therapy (dose 1: Lev 0.58 +/- 0.47 L, Rac 0.44 +/- 0.37 L; P < .01), and patients whose entry (S)-albuterol concentrations were in the highest quartile of those measured. A small and similar proportion of Lev-treated (7.0%) and Rac-treated (9.3%) patients required hospitalization (P = .28). Among patients not on steroids, fewer Lev- than Rac-treated patients required admission (3.8% vs 9.3%, P = .03), as was also the case for patients with high plasma (S)-albuterol concentrations. Asthma relapses (5% in 30 days) were lower than in previous reports and did not differ between groups. **CONCLUSIONS:** This study suggests that early, regular nebulized beta(2)-agonist and systemic corticosteroid therapy may reduce hospitalization and relapse rates in patients with acute severe asthma. Lev was well tolerated and compared favorably with Rac in improving airway function, particularly in those who were not on inhaled or oral corticosteroids and in those who had high plasma (S)-albuterol concentrations at presentation.

Ogunfiditimi, F. (2006). "The role of PAs in robotic-assisted laparoscopic radical prostatectomy." *Jaapa* **19**(3): 57-8, 60-1. [PDF Full-Text](#)

Patel, O. P. and M. R. Simon (2006). "Oculogyric dystonic reaction to escitalopram with features of anaphylaxis including response to epinephrine." *Int Arch Allergy Immunol* **140**(1): 27-9.

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Dystonia-associated features of anaphylaxis, including tongue swelling, and chest and throat tightness, have been rarely reported with selective serotonin reuptake inhibitor (SSRI) use. The patient is a 44-year-old woman who presented with palpitations, diaphoresis, dyspnea, swelling of the lips and tongue, and fixed upward deviation of her right eye following inadvertent ingestion of 20 mg of escitalopram in addition to her usual 10-mg dose. She reported transient resolution of all symptoms after autoinjector aqueous epinephrine administration (0.3 mg), with recurrence of symptoms after 35 min. The patient presented with one prior episode of anaphylactic symptoms and dystonia. She also reported one episode with purely anaphylactic features of swelling of lips and tongue, difficulty breathing and syncope. This case represents a unique dose-dependent episode of escitalopram-associated oculogyric dystonia with anaphylactic features. The transient resolution of the associated features of dystonia with intramuscular epinephrine administration is unique and suggests a common pathophysiology of the dystonic and anaphylactic symptoms.

Payne, S. C. and M. S. Benninger (2006). "Progression of sinus disease in the intubated patient." *Am J Rhinol* **20**(2): 230-4. **Full-Text Not Available / [Click for Article Request Form](#)**

BACKGROUND: Sinus disease in the intubated patient remains a frequent reason behind otolaryngological consultation to the Intensive Care Unit. Previous prospective studies often have been limited to only one computed tomography (CT) scan of the sinuses. The purpose of this study was to verify the development of sinus disease in the orotracheally intubated patient and determine a radiographic pattern of its progression if present. **METHODS:** The charts of all patients admitted to the hospital with a diagnosis of aneurysm or subarachnoid hemorrhage over a 2-year period were evaluated. Patients who were orotracheally intubated with at least one

postintubation CT scan of the head were included. CT scans obtained after the initiation of antibiotics or tracheostomy were excluded. The Lund-Mackay staging system was used to evaluate the scans. **RESULTS:** A total of 50 patients with 172 scans were evaluated. Analysis revealed a significant trend toward increasing severity of radiological sinus disease over the first 7 days of intubation ($p < 0.001$). The presence of a nasogastric tube (NGT) resulted in an increased Lund-Mackay score, but the trend remained significant for patients without an NGT as well. **CONCLUSION:** This study shows that the presence and progression of sinus findings is fairly common in the intubated patient and that although the placement of an NGT increased the rate of development of sinus findings, the lack of one did not preclude sinus disease. Clinical exam remains a more important indicator of disease when evaluating the Intensive Care Unit patient for rhinosinusitis.

Perrotta, A. L. (2006). "Re-treatment of chronic idiopathic thrombocytopenic purpura with rituximab: literature review." *Clin Appl Thromb Hemost* **12**(1): 97-100. **Full-Text Not Available / [Click for Article Request Form](#)**

The aim of this literature review was to identify from published reports, the characteristics and response to rituximab of nine patients with chronic idiopathic thrombocytopenic purpura who had been re-treated after responding to an initial course of therapy. The female/male ratio of re-treated patients was eight, suggesting selection or their suitability for treatment because the female/male ratio of 95 initially treated patients in all published reports between December 1998 and June 2003 was 2. Almost three times as many females responded to the first course of rituximab. All second responses, where recorded, were complete despite two previous partial responses and one minor response. The duration of the second response was at least as durable and more so than the first. Of the nine re-treated patients, the two failures had not undergone splenectomy, yet had achieved a complete response to the first course. All four patients who had previously responded to intravenous immunoglobulin responded to both the initial and subsequent course of rituximab. The influence of prior splenectomy, response to intravenous immunoglobulin, and distinctive patterns of time course until platelet response suggest that there might be different mechanisms of response to rituximab.

Qiu, S., D. S. Rao, S. Palnitkar, and A. M. Parfitt. (2006). "Differences in osteocyte and lacunar density between Black and White American women." *Bone* **38**(1): 130-5. **PDF Full-Text**

We examined the differences in osteocyte and lacunar density between Black and White women, using previously obtained iliac bone biopsies from 34 healthy Black women, aged 21-70 years, and 94 White women, aged 20-73 years. For each subject, the density of osteocytes (Ot.N/B.Ar), empty lacunae (EL.N/B.Ar), and total lacunae (Tt.L.N/B.Ar) and the proportion of osteocyte-occupied lacunae (Ot.N/Tt.L.N) were separately measured in whole trabeculae, superficial bone (<25 microm from the bone surface), and deep bone (>45 microm from the bone surface). Compared with White women, Black women had higher values for osteocytes, empty lacunae, and total lacunae and lower values for percent occupied lacunae in superficial bone and whole trabeculae ($P < 0.01$ to < 0.001). In deep bone there were more osteocytes and total lacunae in Black women, but the other measurements did not differ significantly between the two groups. As in White women, there were fewer osteocytes and total lacunae and more empty lacunae in deep than in superficial bone. The regressions of osteocyte and total lacunar density on age were not significant in Black women, but postmenopausal Black women had fewer osteocytes than premenopausal Black women, and percent occupied lacunae declined significantly with age in whole trabeculae and deep bone, which could only have resulted from osteocyte death. In contrast to White women, there was no inverse relationship between bone formation rate and osteocyte density in superficial bone and the observed bone formation rate was lower than predicted by osteocyte density. We conclude the following: (1) Cancellous bone is made with more osteocytes in Black than in White women, most likely because of diminished apoptosis of osteoblasts; this could contribute to increased bone strength in Black women. (2) In Black women, as in White women, there are fewer osteocytes and total lacunae and more empty lacunae in deep than in superficial bone. (3) There was moderate age-related loss of osteocytes in deep bone in Black women, indicating that osteocyte density depends more on the age of the bone than on the age of the subject. (4) The higher osteocyte density in Black women was not responsible for their lower bone formation rate.

Qureshi, H. S., M. D. Linden, G. Divine, and U. B. Raju. (2006). "E-cadherin status in breast cancer correlates with histologic type but does not correlate with established prognostic parameters." *Am J Clin Pathol* **125**(3): 377-85. **PDF Full-Text**

Our objective was to assess the loss of E-cadherin (EC) as a diagnostic marker or a predictor of prognosis. We stained 276 breast carcinomas with monoclonal antibodies to EC (invasive lobular carcinomas [ILC] and variants, 59; invasive ductal carcinoma and ductal special types [IDC], 204; tubulolobular carcinoma [TLC], 4; and invasive carcinoma [IC], uncertain whether lobular or ductal type, 9). The results were as follows: EC+IDCs, 99.5%; EC-ILCs, 90%; EC+ILCs, 10%; EC+pleomorphic ILCs, 20%; EC-ICs, 44%. All 4 TLCs showed positive tubules while cords were negative. Statistically a correlation of EC loss with a positive diagnosis of ILC was found but there was no correlation with any prognostic tumor variables. A negative EC stain confirms the diagnosis of ILC (specificity, 97.7%; negative predictive value, 96.8%; sensitivity, 88.1%; positive predictive value, 91.2%). EC is helpful in classifying cases with indeterminate histologic features. EC loss is uncommon in nonlobular carcinomas with no correlation to currently established prognostic variables.

Reasons, L. M., S. J. Keteyian, C. A. Brawner, W. D. Weaver, B. Czerska, G. Jacobsen, and J. K. Ehrman. (2006). "Body mass index, functional status and survival in patients with heart failure: 660: 1:15 PM - 1:30 PM." *Med Sci Sports Exerc* **38**(5 Suppl): S19-20. [PDF Full-Text](#)

Robin, A. M., Z. G. Zhang, L. Wang, R. L. Zhang, M. Katakowski, L. Zhang, Y. Wang, C. Zhang, and M. Chopp. (2006). "Stromal cell-derived factor 1alpha mediates neural progenitor cell motility after focal cerebral ischemia." *J Cereb Blood Flow Metab* **26**(1): 125-34. **Full-Text Not Available** / [Click for Article Request Form](#)

In the adult rodent, stroke induces an increase in endogenous neural progenitor cell (NPC) proliferation in the subventricular zone (SVZ) and neuroblasts migrate towards the ischemic boundary. We investigated the role of stromal cell-derived factor 1alpha (SDF-1alpha) in mediating NPC migration after stroke. We found that cultured NPCs harvested from the normal adult SVZ, when they were overlaid onto stroke brain slices, exhibited significantly ($P < 0.01$) increased migration (67.2 ± 25.2 microm) compared with the migration on normal brain slices (29.5 ± 29.5 microm). Immunohistochemistry showed that CXCR 4, a receptor of SDF-1alpha, is expressed in the NPCs and migrating neuroblasts in stroke brain. Blocking SDF-1alpha by a neutralizing antibody against CXCR 4 significantly attenuated stroke-enhanced NPC migration. ELISA analysis revealed that SDF-1alpha levels significantly increased ($P < 0.01$) in the stroke hemisphere (43.6 ± 6.5 pg/mg) when compared with the normal brain (25.2 ± 1.9 pg/mg). Blind-well chamber assays showed that SDF-1alpha enhanced NPC migration in a dose-dependent manner with maximum migration at a dose of 500 ng/mL. In addition, SDF-1alpha induced directionally selective migration. These findings show that SDF-1alpha generated in the stroke hemisphere may guide NPC migration towards the ischemic boundary via binding to its receptor CXCR 4 in the NPC. Thus, our data indicate that SDF-1alpha/CXCR 4 is important for mediating specific migration of NPCs to the site of ischemic damaged neurons.

Rock, J. P., S. Ryu, M. S. Shukairy, F. F. Yin, A. Sharif, F. Schreiber, M. Abdulhak, J. H. Kim, and M. L. Rosenblum. (2006). "Postoperative radiosurgery for malignant spinal tumors." *Neurosurgery* **58**(5): 891-8; discussion 891-8. [PDF Full-Text](#)

OBJECTIVE: Although, as a primary therapy, radiosurgery for spinal tumors is becoming more common in clinical practice and is associated with encouraging clinical results, we wanted to evaluate outcomes after radiosurgery in a series of postoperative patients. **METHODS:** We examined the medical records of 18 postoperative patients who received radiosurgical treatment to their residual spinal tumors: metastatic carcinoma (10), sarcoma (3), multiple myeloma/plasmacytoma (4), and giant cell tumor (1). Marginal radiosurgical doses ranged from 6 to 16 Gy (mean, 11.4 Gy) prescribed to the 90% isodose line. All regions of the spine received treatment: 2 cervical, 15 thoracic, and 1 lumbosacral. The volume of irradiated spinal elements receiving 30, 50, and 80% of the total dose ranged from 0.51 to 11.05, 0.19 to 6.34, and 0.06 to 1.73 cm, respectively. Treatment sessions (i.e., patient in to patient out of the room) varied between 20 and 40 minutes. Follow-up ranged from 4 to 36 months (median, 7 mo). **RESULTS:** Even though significant doses of radiation were delivered to all regions of the spinal cord and nerve roots coincidentally involved in the treatments, only one patient in this series developed progressive symptoms possibly attributable to a toxic effect of the radiosurgery. Of those patients initially presenting with neurological deficits, 92% either remained neurologically stable or improved. **CONCLUSION:** Our observations suggest that radiosurgery as prescribed in this series of postoperative patients with residual spinal tumor is well-tolerated and associated with little to no significant morbidity.

Roth, T. (2006). "Conclusion: Challenges in insomnia treatment." Sleep Med. **Full-Text Not Available** / [Click for Article Request Form](#)

Roth, T. (2006). "Prospects for insomnia treatment." Sleep Med. **Full-Text Not Available** / [Click for Article Request Form](#)

Roth, T., D. Seiden, S. Sainati, S. Wang-Weigand, J. Zhang, and P. Zee. (2006). "Effects of ramelteon on patient-reported sleep latency in older adults with chronic insomnia." Sleep Med **7(4): 312-8.** **Full-Text Not Available** / [Click for Article Request Form](#)

BACKGROUND AND PURPOSE: To assess the efficacy and safety of ramelteon, a selective MT(1)/MT(2) receptor agonist, for chronic insomnia treatment. **PATIENTS AND METHODS:** Randomized, double-blind, placebo-controlled 35-night outpatient trial with weekly clinic visits at multiple centers. Patients include older adults (≥ 65 years; $N=829$) with chronic insomnia. Placebo, ramelteon 4mg, or ramelteon 8mg were taken nightly for five weeks, and patient-reported sleep data were collected using sleep diaries. Primary efficacy was sleep latency at week 1. Sustained efficacy was examined at weeks 3 and 5. Rebound insomnia and withdrawal effects were evaluated during a 7-day placebo run-out. **RESULTS:** Both doses of ramelteon produced statistically significant reductions in sleep latency vs. placebo at week 1 (ramelteon 4mg: 70.2 vs. 78.5min, $P=.008$; ramelteon 8mg: 70.2 vs. 78.5min, $P=.008$). Patients continued to report reduced sleep latency at week 3 with ramelteon 8mg (60.3 vs. 69.3min, $P=.003$), and at week 5 with ramelteon 4mg (63.4 vs. 70.6min, $P=.028$) and ramelteon 8mg (57.7 vs. 70.6min; $P<.001$). Statistically significant increases in total sleep time were observed with ramelteon 4mg at week 1 (324.6 vs. 313.9min, $P=.004$) and week 3 (336.0 vs. 324.3min, $P=.007$) compared with placebo. There was no evidence of significant rebound insomnia or withdrawal effects following treatment discontinuation. The incidence of adverse events was similar among all treatment groups; most were mild or moderate. **CONCLUSIONS:** In older adults with chronic insomnia, ramelteon significantly reduced patient reports of sleep latency over five weeks of treatment with no significant rebound insomnia or withdrawal effects.

Rubin, B., D. J. Reddy, and P. G. Kalman. (2005). "Infringuinal endovascular procedures should be reserved for patients who do not have good open surgical options." Perspect Vasc Surg Endovasc Ther **17(3): 237-44.** **Full-Text Not Available** / [Click for Article Request Form](#)

This article is the result of a debate. The motion proposed was "Infringuinal endovascular procedures should be reserved for patients who do not have good open surgical options." Arguments in favor of the motion were offered by Daniel J. Reddy of Henry Ford Hospital in Detroit, MI, and arguments against the motion were offered by Peter Kalman of Loyola University Medical Center in Maywood, IL.

Sabbah, H. N., R. C. Gupta, S. Rastogi, S. Mishra, Y. Mika, and D. Burkhoff. (2006). "Treating heart failure with cardiac contractility modulation electrical signals." Curr Heart Fail Rep **3(1): 21-4.** **Full-Text Not Available** / [Click for Article Request Form](#)

Major advances have been made over the past two decades in the pharmacologic treatment of chronic heart failure (HF). Angiotensin-converting enzyme inhibitors, beta-blockers, and aldosterone antagonists have had a substantial impact on reducing mortality and morbidity in patients with HF and low left ventricular ejection fraction. These treatments delayed the progression toward advanced intractable HF but did not arrest progressive worsening of the disease. Patients on optimal medical therapy continued to deteriorate, albeit at a much slower pace, ultimately requiring further intervention. This gave rise to a host of device-based therapies that emerged in recent years to address this unmet need. Device therapies such as cardiac resynchronization, the CorCap cardiac support device (Acorn Cardiovascular, Inc., St. Paul, MN), and the OPTIMIZER System (Impulse Dynamics USA, Inc., Orangeburg, NY) are a few examples. This review addresses the progress made to date in the development and implementation of cardiac contractility modulation (CCM) as a device-based therapy for the treatment of patients with advanced HF. Treatment of patients with HF using CCM electrical signals is at present an investigational form of therapy.

Saval, M. A., D. J. Kerrigan, K. M. Ophaug, J. K. Ehrman, and S. J. Keteyian. (2006). "Knee extensor strength and endurance correlate with peak treadmill oxygen consumption in heart failure patients: 662: 1:45 PM - 2:00 PM." Med Sci Sports Exerc **38**(5 Suppl): S20. [PDF Full-Text](#)

Schairer, J. R., K. A. Nour, J. K. Ehrman, and S. J. Keteyian. (2006). "Cardiovascular - Chest Pain with ST Elevation on Exercise Test: 1186: 9:20 AM - 9:40 AM." Med Sci Sports Exerc **38**(5 Suppl): S141. [PDF Full-Text](#)

Shah, R. A., S. Khanal, and A. Kugelmass. (2006). "Spontaneous late thrombolysis of an occluded saphenous vein graft subsequent to acute myocardial infarction treated with percutaneous coronary intervention to the native culprit vessel." J Interv Cardiol **19**(2): 178-82. **Full-Text Not Available / [Click for Article Request Form](#)**

A 67-year-old male with prior history of myocardial infarction and coronary artery bypass grafting (individual vein grafts to the left anterior descending artery [LAD] and right coronary artery) presented with an acute anterior ST elevation myocardial infarction and cardiogenic shock. The vein graft to the LAD was occluded with heavy thrombus burden and there was severe native CAD. Given the degree of thrombus burden and other anatomic considerations, percutaneous intervention with stenting was performed to the native proximal LAD. Three months later, after complaining of atypical chest pain, repeat angiogram revealed a spontaneous widely patent vein graft to the LAD and occluded proximal LAD.

Shen, L. H., Y. Li, J. Chen, J. Zhang, P. Vanguri, J. Borneman, and M. Chopp. (2006). "Intracarotid transplantation of bone marrow stromal cells increases axon-myelin remodeling after stroke." Neuroscience **137**(2): 393-9. [PDF Full-Text](#)

The present study investigates the induction of axon and myelin remodeling as a possible mechanism by which treatment of stroke with bone marrow stromal cells improves neurological functional recovery. Adult male Wistar rats were subjected to 2 h of middle cerebral artery occlusion, followed by an injection of 2×10^6 rat bone marrow stromal cells or phosphate-buffered saline into the internal carotid artery 24 h later. Animals were killed at 28 days after stroke. Functional tests, histo- and immunohistochemical staining were performed. Significant functional recovery was found after bone marrow stromal cell administration in all the three tests performed (modified neurological severity score, adhesive-removal and corner tests). Bone marrow stromal cell treatment markedly increased vessel sprouting, synaptophysin expression and NG2 positive cell numbers and density in the cortical peri-infarct area. In bone marrow stromal cell-treated rats, the number of Ki-67 positive proliferating cells and oligodendrocyte precursor cells in the corpus callosum increased significantly in concert with the enhancement of the areas of the corpus callosum in both hemispheres. These results suggest that bone marrow stromal cells facilitate axonal sprouting and remyelination in the cortical ischemic boundary zone and corpus callosum, which may underlie neurological functional improvement caused by bone marrow stromal cell treatment.

Slining, J. M. (2006). "Women's Role in Pharmacy Practice in the Year 2000." Ann Pharmacother **40**(5): 964-8. [PDF Full-Text](#)

Subramanian, B., A. Nakeff, K. Tenney, P. Crews, L. Gunatilaka, and F. Valeriote. (2006). "A new paradigm for the development of anticancer agents from natural products." J Exp Ther Oncol **5**(3): 195-204. **Full-Text Not Available / [Click for Article Request Form](#)**

A novel pharmacology paradigm has been developed which quickly and efficiently moves prospective anticancer drugs from the discovery phase through pharmacology testing and into therapeutic trial assessment. Following discovery, the drug is first assessed in a clonogenic assay which determines the cytotoxic effect of different concentrations of the drug at 3 different exposure durations: 2h, 24h and continuous (168 h). Second, pharmacokinetic information is obtained in both plasma and tumor for the drug administered at the maximum tolerated dose given intravenously. The first study defines the time-concentration profile required to obtain a specific cell survival for the tumor cells; the second study determines the concentration-time profile that can be

obtained in both plasma and tumor at the maximum tolerated dose of the drug. The integration of this information determines whether a successful therapeutic trial is possible. Only when a drug shows therapeutic efficacy is a proteomics-based mechanism of action study initiated. Two drugs have been assessed in this paradigm: salicortin and fascalysin A.

Trick, G. L., P. Edwards, U. Desai, and B. A. Berkowitz. (2006). "Early supernormal retinal oxygenation response in patients with diabetes." *Invest Ophthalmol Vis Sci* **47**(4): 1612-9. [PDF Full-Text](#)

PURPOSE: To determine whether the human retinal oxygenation response (deltaPO₂) to a hyperoxic provocation is abnormal in patients with type I diabetes. **METHODS:** Magnetic resonance imaging (MRI) was used to measure deltaPO₂ during 100% oxygen breathing in patients with type I diabetes who had either no clinically detectable retinopathy (n = 5) or mild to moderate background diabetic retinopathy (BDR; n = 5) and in age-matched healthy control subjects (n = 7). **RESULTS:** Both the patients with diabetes and the control subjects exhibited a significant (P < 0.05) increase in the preretinal vitreous signal intensity on changing from room air breathing to oxygen inhalation (i.e., 5 minutes). However, only diabetic patients demonstrated significant (P < 0.05) increases in deltaPO₂ between measurements made at 5 minutes of oxygen inhalation and measurements at longer durations of hyperoxia (15, 25, and 35 minutes). Furthermore, deltaPO₂ was significantly (P < 0.05) greater in patients with diabetes than in control subjects, but there was no significant difference in deltaPO₂ (P > 0.05) between patients with diabetes, with or without retinopathy. Age and deltaPO₂ correlated significantly (P < 0.05) in control subjects but not in patients with diabetes. In control subjects, deltaPO₂ was relatively uniform panretinally, whereas in the diabetic group, changes in oxygenation response were spatially inhomogeneous. **CONCLUSIONS:** These results demonstrate, for the first time, that MRI deltaPO₂ detects a significant supernormal retinal oxygenation response in patients with type I diabetes, even before the appearance of retinopathy. This study raises the possibility of using MRI measurements of deltaPO₂ to monitor therapeutic efficacy in human trials.

Tuchinda, C., S. Srivannaboon, and H. W. Lim. (2006). "Photoprotection by window glass, automobile glass, and sunglasses." *J Am Acad Dermatol* **54**(5): 845-54. [PDF Full-Text](#)

In daily activity, much time is spent indoors and in vehicles. Although the adverse effect of ultraviolet (UV) radiation is now well recognized and active public education programs on photoprotection have been undertaken, the role of window glass in photoprotection has been rarely addressed. It has been known for some time that window glass filters out UVB and transmits UVA and visible light. Recent developments in the glass industry have resulted in glass that provides broad UV protection without the historically associated loss of visible light transmission. Factors affecting UV-protective properties of glass are glass type, glass color, interleave between glass, and glass coating. In this article, photoprotection by window glass, automobile glass, and sunglasses is reviewed.

Undrovinas, A. I., L. Belardinelli, N. A. Undrovinas, and H. N. Sabbah. (2006). "Ranolazine improves abnormal repolarization and contraction in left ventricular myocytes of dogs with heart failure by inhibiting late sodium current." *J Cardiovasc Electrophysiol* **17** Suppl 1: S169-S177. **Full-Text Not Available / [Click for Article Request Form](#)**

BACKGROUND: Ventricular repolarization and contractile function are frequently abnormal in ventricular myocytes from human failing hearts as well as canine hearts with experimentally induced heart failure (HF). These abnormalities have been attributed to dysfunction involving various steps of the excitation-contraction coupling process, leading to impaired intracellular sodium and calcium homeostasis. We previously reported that the slow inactivating component of the Na⁽⁺⁾ current (late I_(Na)) is augmented in myocytes from failing hearts, and this appears to play a significant role in abnormal ventricular myocytes repolarization and function. We tested the effect of ranolazine, a novel drug being developed to treat angina, on (1) action potential duration (APD), (2) peak transient and late I_(Na) (I_(NaT) and I_(NaL), respectively), (3) early afterdepolarizations (EADs), and (4) twitch contraction (TC), including after contractions and contracture. **METHODS:** Myocytes were isolated from the left ventricle of normal dogs and of dogs with chronic HF caused by multiple sequential intracoronary micro-embolizations. I_(NaT) and I_(NaL) were recorded using conventional whole-cell patch-clamp techniques. APs were recorded using the beta-escin perforated patch-clamp configuration at frequencies of 0.25 and 0.5 Hz. TCs were recorded using an edge movement detector at stimulation frequencies ranging from 0.5 to 2.0 Hz. **RESULTS:**

Ranolazine significantly ($P < 0.05$) and reversibly shortened the APD of myocytes stimulated at either 0.5 or 0.25 Hz in a concentration-dependent manner. At a stimulation frequency of 0.5 Hz, 5, 10, and 20 μM ranolazine shortened the APD(90) (APD measured at 90% repolarization) from 516 ± 51 to 304 ± 22 , 212 ± 34 and 160 ± 11 ms, respectively, and markedly decreased beat-to-beat variability of APD(90), EADs, and dispersion of APDs. Ranolazine preferentially blocked I(NaL) relative to I(NaT) in a state-dependent manner, with an approximately 38-fold greater potency against I(NaL) to produce tonic block ($\text{IC}(50) = 6.5 \mu\text{M}$) than I(NaT) ($\text{IC}(50) = 294 \mu\text{M}$). When we evaluated inactivated state blockade of I(NaL) from the steady-state inactivation mid-potential shift using a theoretical model, ranolazine was found to bind more tightly to the inactivated state than the resting state of the sodium channel underlying I(NaL), with apparent dissociation constants $K(\text{dr}) = 7.47 \mu\text{M}$ and $K(\text{di}) = 1.71 \mu\text{M}$, respectively. TCs of myocytes stimulated at 0.5 Hz were characterized by an initial spike followed by a dome-like after contraction, which was observed in 75% of myocytes from failing hearts and coincided with the long AP plateau and EADs. Ranolazine at 5 and 10 μM reversibly shortened the duration of TCs and abolished the after contraction. When the rate of myocyte stimulation was increased from 1.0 to 2.0 Hz, there was a progressive increase in diastolic "tension," that is, contracture. Ranolazine at 5 and 10 μM reversibly prevented this frequency-dependent contracture.

Varelas, P. N. and M. Spanaki (2006). "Management of seizures in the critically ill." Neurologist **12**(3): 127-39. [PDF Full-Text](#)

Seizures in a critically ill patient are not infrequent phenomena. Physicians are perplexed by the wide range of possible cranial or extracranial etiologies, alerted by the risk for further crucial organ compromise if seizures recur, and confused about the treatment options in an environment rich in complex drug interactions and multiple organ dysfunction. The advent of an armamentarium containing multiple new antiepileptic medications complicates the situation further, since several of them have less known mechanisms of action, side effects, or interactions with other intensive care unit (ICU) medications. This review contains useful information regarding the most common etiologies and treatment options for intensivists, consulting neurologists, neurosurgeons, or other specialized physicians treating ICU patients with seizures.

Velanovich, V., T. Kamolz, R. Pointner, and S. Contini. (2006). "Qualitative analysis of the expectations of antireflux surgical outcomes of patients from different nationalities." Dis Esophagus **19**(2): 88-93. **Full-Text Not Available / [Click for Article Request Form](#)**

Patient-reported outcomes have grown in importance in assessing the value of a variety of treatments. One of the methods of assessing patient-reported outcomes is qualitative analysis. The purpose of this study was to assess if qualitative analysis can be used to assess patient expectations for antireflux surgery in different nationalities. Patients referred for antireflux surgery (ARS) in the US, Austria and Italy were prospectively studied. Preoperatively, they were asked: (i) 'How do you expect the surgery to affect your symptoms?'; (ii) 'What do you expect the possible complications or side effects to be?' These patients then underwent open or laparoscopic antireflux surgery. At 2-3 months postoperatively, they were asked: (i) 'Are you satisfied with your surgery? If so, why? If not, why not?'; (ii) 'Did your surgery meet your expectations? If not, why not?' Twenty patients in the US, 24 in Austria, and 18 in Italy completed the study. Preoperatively, there were significant differences between the patients in demographics and objective measurements of GERD. Symptomatic relief was the most common expectation. There was variation in question #2, with Austrian and Italian patients more likely to mention conversion and postoperative side effects. Postoperatively, 90% of American, 88% of Austrian, and 89% of Italian patients were satisfied. Causes for dissatisfaction were postoperative complications, symptomatic recurrences, or side effects. Ninety percent of American, 96% of Austrian, and 94% of Italian patients said that their expectations were met. Patients who did not mention the possibility of side effects or complications were more likely to be dissatisfied. Qualitative analysis is a useful tool in assessing patient expectations. Expectations were remarkably similar. Patients who did not mention postoperative adverse events as possibilities preoperatively were more likely to be dissatisfied.

Verlander, J. W., Y. H. Kim, W. Shin, T. D. Pham, K. A. Hassell, W. H. Beierwaltes, E. Green, L. A. Everett, S. W. Matthews, and S. M. Wall. (2006). "Dietary Cl⁻ restriction upregulates pendrin expression within the apical plasma membrane of type B intercalated cells." Am J Physiol Renal Physiol. [PDF Full-Text](#)

Pendrin, encoded by *Slc26a4*, is a Cl⁻/HCO₃⁻ exchanger expressed in the apical region of type B and non-A, non-B intercalated cells, which regulates renal NaCl excretion. Dietary Cl⁻ restriction upregulates total pendrin protein expression. Whether the subcellular expression of pendrin and whether the apparent vascular volume contraction observed in *Slc26a4* null mice are Cl⁻-dependent, but Na⁺-independent, is unknown. Thus, the subcellular distribution of pendrin and its role in acid-base and fluid balance were explored using immunogold cytochemistry and balance studies of mice ingesting a NaCl-replete or a Na⁺-replete, Cl⁻ restricted diet, achieved through substitution of NaCl with NaHCO₃. Boundary length and apical plasma membrane pendrin label density each increased by ~60-70% in type B intercalated cells, but not in non-A, non-B cells, whereas pendrin immunolabel density increased ~60% in non-A, non-B intercalated cells, but not in type B cells. Following either NaCl restriction or Cl⁻ restriction alone, *Slc26a4* null mice excrete more Cl⁻ and developed a higher arterial pH than pair-fed wild type mice. Conclusions: 1. Following dietary Cl⁻ restriction, apical plasma membrane pendrin immunolabel increases in type B intercalated cells. 2. Pendrin is critical in the regulation of renal Cl⁻ excretion and arterial pH during dietary Cl⁻ restriction.

Wegienka, G., S. Havstad, and J. L. Kelsey. (2006). "Menopausal Hormone Therapy in a Health Maintenance Organization before and after Women's Health Initiative Hormone Trials Termination." *J Womens Health (Larchmt)* **15**(4): 369-78. **Full-Text Not Available / [Click for Article Request Form](#)**

Background: In July 2002, the Women's Health Initiative (WHI) published results that led to early termination of the randomized controlled trial of estrogen plus progestin in postmenopausal women with an intact uterus. Subsequently, the trial of estrogen only also was terminated early, and the results were published in April 2004. The present study examines the impact of both sets of results on menopausal hormone therapy (MHT) prescription patterns, as well as the characteristics of women who did and did not change their MHT behavior after publication of results. Methods: We examined the number of MHT prescriptions filled in the months before and after each set of results was published, using claims data from 24,446 women aged 50-79 years continuously enrolled in a health maintenance organization (HMO) at Henry Ford Health System from January 2000 through December 2004. Results: After July 2002, a statistically significant ($p < 0.05$) drop occurred in the rate of MHT prescriptions filled; 29% of the women stopped MHT for at least 4 months, but 24% of these women resumed use by December 2004. Successful stoppers tended to be older. Twentyone percent of users in April 2004 stopped in May 2004 for at least 4 months; 25% of these had restarted by December. Women continued to initiate MHT after July 2002, but at lower rates in 2003 and 2004 (73% and 77% decreases, respectively, compared with 2001). The types of MHT prescriptions obtained by new users changed after 2001: fewer initiated MHT with oral Premarin (Wyeth, St. David's, PA) and Prempro or Premphase (Wyeth-Ayerst, Philadelphia, PA), and more initiated MHT with Premarin and Estrace (Warner Chilcott, Rockaway, NJ) creams. Conclusions: Regardless of the goals of the WHI study, the publication of results on estrogen plus progestin in July 2002 impacted overall rates of MHT use, as did, to a lesser extent, the estrogen only results published in May 2004. Although women continued to initiate MHT after the results were published, they were less likely to use the formulations from the WHI and instead used formulations for which there is less information about effectiveness and long-term health consequences.

Yang, H., M. Preston, M. Chopp, F. Jiang, X. Zhang, and T. Schallert. (2006). "Mass-Related Traumatic Tissue Displacement and Behavior: A Screen for Treatments that Reduces Harm to Bystander Cells and Recovery of Function." *J Neurotrauma* **23**(5): 721-32. **Full-Text Not Available / [Click for Article Request Form](#)**

In this study, we focused on a preclinical model of brain compression injury that has relevance to pathological conditions such as tumor, hematoma, blood clot, and intracerebral bony fragment. We investigated behavioral impairment as a result of rapid-onset small mass, and the factors involved in lesion formation and neuroplasticity. An epidural bead implantation method was adopted. Two sizes (1.5 mm and 2.0 mm thick) of hemisphere-shaped beads were used. The beads were implanted into various locations over the sensorimotor cortex (SMC-anterior, middle and posterior). The effects of early versus delayed bead removal were examined to model clinical neurosurgical or other treatment procedures. Forelimb and hind-limb behavioral deficits and recovery were observed, and histological changes were quantified to determine brain reaction to focal compression. Our results showed that the behavioral deficits of compression were influenced by the location, timing of compression release, and magnitude of compression. Even persistent compression by the thicker bead (2.0 mm) caused only minor behavioral deficits, followed by fast recovery within a week in most animals, suggesting a mild lesion pattern for

this model. Brain tissue was compressed into a deformed shape under pressure with slight tissue damage, evidenced by pathological evaluation on hematoxylin and eosin (H&E)- and TUNEL-stained sections. Detectable but not severe behavioral dysfunction exhibited by this model makes it particularly suitable for direct assessment of adverse effects of interventions on neuroplasticity after brain compression injury. This model may permit development of treatment strategies to alleviate brain mass effects, without disrupting neuroplasticity.

Yang, H., X. Zhang, M. Chopp, F. Jiang, and T. Schallert. (2006). "Local fluorouracil chemotherapy interferes with neural and behavioral recovery after brain tumor-like mass compression." *Behav Brain Res*. **Full-Text Not Available** / [Click for Article Request Form](#)

In this study, we investigated the impact of intracerebral delivery of chemotherapy on functional recovery from focal cortical tissue displacement, characteristic of brain tumors. Unilateral focal brain compression was induced by epidural implantation of an inverted hemisphere-shaped bead over the sensorimotor cortex. Microinjections of a total of 1mg chemoagent fluorouracil or the same volume of saline were made into the compressed cortex. Behavioral tests of forelimb sensorimotor function were conducted during 4 weeks' observation. Rats subjected to any of the three types of lesions, saline microinjection plus cortical compression, chemoagent microinjection alone, or chemoagent microinjection combined with cortical compression, demonstrated significant behavioral deficits in several sensorimotor tasks, compared with saline-microinjected control animals. In placing tests, behavioral deficits elicited by each single treatment were worsened by combined treatment with chemoagent microinjection and focal cortical compression. Concurrently, local delivery of chemoagent into the compressed cortex induced increased cortical tissue loss, necrosis and apoptosis. These data indicate that local chemotherapy exacerbates compression-induced neurological impairment, and a model of controlled focal cortical compression may provide a valuable means to improve anti-cancer therapeutic designs with reduced deterioration of brain function.

Zarbo, R. J. (2006). "Determining customer satisfaction in anatomic pathology." *Arch Pathol Lab Med* **130**(5): 645-9. [PDF Full-Text](#)

CONTEXT: Measurement of physicians' and patients' satisfaction with laboratory services has become a standard practice in the United States, prompted by national accreditation requirements. Unlike other surveys of hospital-, outpatient care-, or physician-related activities, no ongoing, comprehensive customer satisfaction survey of anatomic pathology services is available for subscription that would allow continual benchmarking against peer laboratories. Pathologists, therefore, must often design their own local assessment tools to determine physician satisfaction in anatomic pathology. OBJECTIVE: To describe satisfaction survey design that would elicit specific information from physician customers about key elements of anatomic pathology services. DESIGN: The author shares his experience in biannually assessing customer satisfaction in anatomic pathology with survey tools designed at the Henry Ford Hospital, Detroit, Mich. Benchmarks for physician satisfaction, opportunities for improvement, and characteristics that correlated with a high level of physician satisfaction were identified nationally from a standardized survey tool used by 94 laboratories in the 2001 College of American Pathologists Q-Probes quality improvement program. RESULTS: In general, physicians are most satisfied with professional diagnostic services and least satisfied with pathology services related to poor communication. CONCLUSIONS: A well-designed and conducted customer satisfaction survey is an opportunity for pathologists to periodically educate physician customers about services offered, manage unrealistic expectations, and understand the evolving needs of the physician customer. Armed with current information from physician customers, the pathologist is better able to strategically plan for resources that facilitate performance improvements in anatomic pathology laboratory services that align with evolving clinical needs in health care delivery.

Zhang, L., Z. G. Zhang, X. Liu, A. Hozeska, N. Stagliano, W. Riordan, M. Lu, and M. Chopp. (2006). "Treatment of embolic stroke in rats with bortezomib and recombinant human tissue plasminogen activator." *Thromb Haemost* **95**(1): 166-73. **Full-Text Not Available** / [Click for Article Request Form](#)

Stroke elicits a progressive vascular dysfunction, which contributes to the evolution of brain injury. Thrombolysis with tissue plasminogen activator (tPA) promotes adverse vascular events that limit the therapeutic window of stroke to three hours. Proteasome inhibitors reduce vascular thrombotic and inflammatory events, and consequently protect vascular function. The present study evaluated the neuroprotective effect of bortezomib, a

potent and selective inhibitor of the proteasome, alone and in combination with delayed thrombolytic therapy on a rat model of embolic focal cerebral ischemia. Treatment with bortezomib reduces adverse cerebrovascular events including secondary thrombosis, inflammatory responses, and blood brain barrier (BBB) disruption, and hence reduces infarct volume and neurological functional deficit when administered within 4 h after stroke onset. Combination of bortezomib and tPA extends the thrombolytic window for stroke to 6 h, which is associated with the improvement of vascular patency and integrity. Real time RT-PCR of endothelial cells isolated by laser-capture microdissection from brain tissue and Western blot analysis showed that bortezomib upregulates endothelial nitric oxide synthase (eNOS) expression and blocks NF-kappaB activation. These results demonstrate that bortezomib promotes eNOS dependent vascular protection, and reduces NF-kappaB dependent vascular disruption, all of which may contribute to neuroprotection after stroke.

Zhuo, J. L. (2006). "Intracrine renin and angiotensin II: a novel role in cardiovascular and renal cellular regulation." J Hypertens **24**(6): 1017-20. [PDF Full-Text](#)

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