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

Ananthasubramaniam, K. (2005). "Clinical and echocardiographic features of aorto-atrial fistulas." *Cardiovasc Ultrasound* 3(1): 1. **Full-Text Not Available** / [Click for Article Request Form](#)

Aorto-atrial fistulas (AAF) are rare but important pathophysiologic conditions of the aorta and have varied presentations such as acute pulmonary edema, chronic heart failure and incidental detection of the fistula. A variety of mechanisms such as aortic dissection, endocarditis with pseudoaneurysm formation, post surgical scenarios or trauma may precipitate the fistula formation. With increasing survival of patients, particularly following complex aortic reconstructive surgeries and redo valve surgeries, recognition of this complication, its clinical features and echocardiographic diagnosis is important. Since physical exam in this condition may be misleading, echocardiography serves as the cornerstone for diagnosis. The case below illustrates aorto-left atrial fistula formation following redo aortic valve surgery with slowly progressive symptoms of heart failure. A brief review of the existing literature of this entity is presented including emphasis on echocardiographic diagnosis and treatment.

Angoa-Perez, M., H. Jiang, A. I. Rodriguez, C. Lemini, R. A. Levine, and S. Rivas-Arancibia. (2006). "Estrogen counteracts ozone-induced oxidative stress and nigral neuronal death." *Neuroreport* 17(6): 629-633. [PDF Full-Text](#)

Oxidative stress is implicated in the premature death of dopamine neurons in substantia nigra in Parkinson's disease. The incidence of Parkinson's disease is higher in men than in women, and estrogen may provide neuroprotection against oxidative damage. We examined the protective effects of estrogen on rat nigral death after chronic ozone inhalation. Ozone inhalation produced impaired nigral cell morphology and loss of dopamine neurons in ovariectomized rats. This was counteracted after 60 days of 17beta-estradiol treatment, when blood levels were highest. These results indicate that ozone exposure may be a useful Parkinson's disease model and neuroprotection afforded by 17beta-estradiol is dependent on the high levels achieved after its prolonged administration.

Artinian, V., H. Krayem, and B. DiGiovine. (2006). "Effects of early enteral feeding on the outcome of critically ill mechanically ventilated medical patients." *Chest* 129(4): 960-7. [PDF Full-Text](#)

STUDY OBJECTIVES: To determine the impact of early enteral feeding on the outcome of critically ill medical patients. DESIGN: Retrospective analysis of a prospectively collected large multi-institutional ICU

database. PATIENTS: A total of 4,049 patients requiring mechanical ventilation for > 2 days. MEASUREMENTS AND RESULTS: Patients were classified according to whether or not they received enteral feeding within 48 h of mechanical ventilation onset. The 2,537 patients (63%) who did receive enteral feeding were labeled as the "early feeding group," and the remaining 1,512 patients (37%) were labeled as the "late feeding group." The overall ICU and hospital mortality were lower in the early feeding group (18.1% vs 21.4%, $p = 0.01$; and 28.7% vs 33.5%, $p = 0.001$, respectively). The lower mortality rates in the early feeding group were most evident in the sickest group as defined by quartiles of severity of illness scores. Three separate models were done using each of the different scores (acute physiology and chronic health evaluation II, simplified acute physiology score II, and mortality prediction model at time 0). In all models, early enteral feeding was associated with an approximately 20% decrease in ICU mortality and a 25% decrease in hospital mortality. We also analyzed the data after controlling for confounding by matching for propensity score. In this analysis, early feeding was again associated with decreased ICU and hospital mortality. In all adjusted analysis, early feeding was found to be independently associated with an increased risk of ventilator-associated pneumonia (VAP) developing. CONCLUSION: Early feeding significantly reduces ICU and hospital mortality based mainly on improvements in the sickest patients, despite being associated with an increased risk of VAP developing. Routine administration of such therapy in medical patients receiving mechanical ventilation is suggested, especially in patients at high risk of death.

Attallah, N., Y. Osman-Malik, S. Frinak, and A. Besarab. (2006). "Effect of intravenous ascorbic acid in hemodialysis patients with EPO-hyporesponsive anemia and hyperferritinemia." *Am J Kidney Dis* 47(4): 644-54. [PDF Full-Text \(User Name – sladen / Password – library1\)](#)

BACKGROUND: Although erythropoietin (EPO)-hyporesponsive anemia in hemodialysis patients most commonly results from iron deficiency, the contributory role of chronic inflammation and oxidative stress in its pathogenesis is poorly understood. We conducted an open-label prospective study to assess the effect of vitamin C, an antioxidant, on EPO-hyporesponsive anemia in hemodialysis patients with unexplained hyperferritinemia. METHODS: Forty-six of 262 patients in an inner-city hemodialysis center met the inclusion criteria (administration of intravenous iron and EPO for > or = 6 months at a dose > or = 450 U/kg/wk, average 3-month hemoglobin [Hb] level < or = 11.0 g/dL [$< or = 110$ g/L], ferritin level > or = 500 ng/mL (microg/L), and transferrin saturation [TSAT] < or = 50%). Patients were excluded if they had a clear explanation for the EPO hyporesponsiveness. Four patients refused to participate. The remaining patients were randomly assigned; 20 patients to receive standard care and 300 mg of intravenous vitamin C with each dialysis session (group 1) and 22 patients to receive standard care only (group 2). Study duration was 6 months. During the study, 1 patient from group 1 was removed (upper gastrointestinal bleeding) from final analysis. Monthly assessment included Hb level, mean corpuscular volume, iron level, iron-binding capacity, ferritin level, TSAT, and Hb content in reticulocytes. In addition, bioactive parathyroid hormone, aluminum, C-reactive protein (CRP), and liver enzymes were measured every 3 months. RESULTS: Age, sex, race, and time on dialysis therapy were similar in both groups. At 6 months, Hb levels significantly increased from 9.3 to 10.5 g/dL (93.0 to 105.0 g/L) in group 1, but not group 2 (9.3 to 9.6 g/dL [93.0 to 96.0 g/L]; $P = 0.0001$). Similarly, TSAT increased from 28.9% to 37.3% in group 1, but not group 2 (28.7% to 29.3%; $P = 0.0001$). EPO dose (477 to 429 versus 474 to 447 U/kg/wk), iron-binding capacity (216 to 194 versus 218 to 257 microg/dL [38.7 to 34.7 versus 39 to 46 micromol/L]), and CRP level (2.8 to 0.9 versus 2.8 to 2.2 mg/dL) decreased significantly in group 1, but not in controls. Changes in Hb content in reticulocytes and ferritin level also were statistically significant in group 1. There was no change in bioactive parathyroid hormone levels. Although serum iron levels and intravenous iron doses changed within each group, changes were equal between the 2 groups. CONCLUSION: In hemodialysis patients with refractory anemia and hyperferritinemia, vitamin C improved responsiveness to EPO, either by augmenting iron mobilization from its tissue stores or through antioxidant effects.

Austin, M. M. (2006). "Diabetes educators: partners in diabetes care and management." *Endocr Pract* 12 Suppl 1: 138-41. [Full-Text Not Available / Click for Article Request Form](#)

OBJECTIVE: To promote the role of the diabetes educator as an important team member in conjunction with the patient and other clinicians in optimizing diabetes management. METHODS: The goal of the diabetes educator in facilitating changes in patient behavior is reviewed, and current trends and strategies

for improvement of outcomes by means of diabetes education are outlined. RESULTS: The American Association of Diabetes Educators (AADE) is a multidisciplinary group of healthcare professionals dedicated to the professional growth and development of personnel who are responsible for diabetes education. Diabetes management is best addressed by using a team approach in a patient-centered care environment. Diabetes education encompasses more than the dissemination of information; the goal is to facilitate changes in specific behaviors relating to both therapy and lifestyle that support good diabetes management and improved clinical outcomes. Diabetes educators currently frame their intervention on the basis of the AADE 7 Self-Care Behaviors: (1) healthful eating, (2) being active, (3) monitoring, (4) taking medication, (5) problem-solving, (6) healthful coping, and (7) reducing risks. Diabetes education is underutilized; approximately 60% to 70% of patients with diabetes have not received training in diabetes self-management. Diabetes educators are trained to identify and help overcome barriers to optimal diabetes care. CONCLUSION: Individual patients and the overall health-care system will benefit when physicians and other health-care providers collaborate with diabetes educators to ensure that patients receive the information, training, and support needed to facilitate effective diabetes self-management.

Badani, K. K., A. K. Hemal, J. O. Peabody, and M. Menon. (2006). "Robotic radical prostatectomy: the Vattikuti Urology Institute training experience." World J Urol. **Full-Text Not Available** / [Click for Article Request Form](#)

Robotic radical prostatectomy is increasingly becoming a popular surgical treatment modality for men with clinically localized prostate cancer. Establishing a robotic prostatectomy program is a tremendous undertaking for any institution requiring both financial support and a dedicated operating room team. A structured approach to learning robotics is paramount in order to successfully start a program while optimizing the learning curve to master the technique and minimize peri-operative complications. We describe our own experience in establishing a robotics program to accomplish a safe and effective operation. In addition, we describe the steps utilized in order to teach our structured approach to other practitioners and institutions around the world. Robotic surgery can be taught to experienced open, as well as, laparoscopic surgeons, and incorporated into residency and fellowship training using this structured approach to learning.

Barton, K. N., H. Stricker, A. Kolozsvary, R. Kohl, G. Heisey, T. N. Nagaraja, G. Zhu, M. Lu, J. H. Kim, S. O. Freytag, and S. L. Brown. (2006). "Polyethylene glycol (molecular weight 400 DA) vehicle improves gene expression of adenovirus mediated gene therapy." J Urol **175**(5): 1921-5. **Full-Text Not Available** / [Click for Article Request Form](#)

PURPOSE: A significant limitation of adenoviral mediated suicide gene therapy is poor gene distribution in vivo. The choice of vehicle has been demonstrated to affect the level of adenoviral delivered gene transduction. We examined the hypotheses that 1) adenovirus suspended in PEG400 improves gene expression in the naive canine prostate model, 2) improved transgene expression with PEG400 results in improved tumor control and 3) vehicle affects the initial adenoviral spread from a single intratumor injection. MATERIALS AND METHODS: The magnitude and volume of gene expression were measured 24 hours following intraprostatic injection of adenovirus suspended in PEG400 (12.5% weight per volume) or saline as vehicle. Tumor growth delay was measured in mice bearing human tumor xenografts following the injection of adenovirus in PEG400 and saline. The initial spread of adenovirus was measured by confocal microscopy following a single injection of fluorescently labeled adenoviral particles in human tumor xenografts using each vehicle. RESULTS: Adenovirus suspended in PEG400 provided an average of twice the level of gene expression in the canine prostate and significantly better tumor control relative to saline in preclinical tumor models ($p = 0.046$ and 0.036 , respectively). The initial spread of adenovirus with PEG400 was superior to that of adenovirus in saline and the latter was largely limited to the needle tract. CONCLUSIONS: Adenoviral gene therapy vectors suspended in PEG400 results in improved tumor control because of greater initial adenoviral spread, and the increased volume and magnitude of gene expression in vivo.

Billecke, C., I. Malik, A. Movsisyan, S. Sulghani, A. Sharif, T. Mikkelsen, N. P. Farrell, and O. Bogler. (2006). "Analysis of glioma cell platinum response by metacomparison of two-

dimensional chromatographic proteome profiles." *Mol Cell Proteomics* 5(1): 35-42. **Full-Text Not Available / [Click for Article Request Form](#)**

Successful clinical development of cancer treatments is aided by the development of molecular markers that allow the identification of patients likely to respond. In the case of broadly cytotoxic drugs, such as the multinuclear series of platinum chemotherapeutic agents that we are evaluating for the treatment of glioma, one route to marker identification is proteomic profiling. We are using the two-dimensional chromatography system, the ProteomeLab PF2D, to compare proteomic profiles of glioma cells in culture before and after drug treatment. The existing software tools allowed the rapid identification of peaks increased by treatment of a given drug as compared with control untreated cells. To compare across these pairs, we developed new software, called the MetaComparison Tool (MCT). The MCT uses the chromatographic characteristics of peaks as identifiers, an approach that was validated by mass spectrometry of two independent isolations of a peak, from cells that were treated with two different platinum compounds. The MCT made it possible to rapidly query whether a given peak responded to more than one treatment and so allowed the identification of peaks that were specific to a given drug. As a result, this analysis greatly reduced the list of peaks whose isolation and downstream analysis by mass spectrometry is warranted, accelerating the search for protein markers of response.

Brawner, C. A., M. A. Vanzant, J. K. Ehrman, C. Foster, J. P. Porcari, A. J. Kelso, and S. J. Keteyian. (2006). "Guiding Exercise Using the Talk Test Among Patients With Coronary Artery Disease." *J Cardiopulm Rehabil* 26(2): 72-75. **[PDF Full-Text](#)**

Cankovic, M., M. D. Linden, and R. J. Zarbo. (2006). "Use of microsatellite analysis in detection of tumor lineage as a cause of death in a liver transplant patient." *Arch Pathol Lab Med* 130(4): 529-32. **[PDF Full-Text](#)**

Malignant tumors are a significant cause of long-term morbidity and mortality in allograft recipients. Most solid tumors in transplant recipients are assumed to arise de novo in the setting of chronic immunosuppressive therapy; however, there have been instances in which malignant tumors have been transplanted in donated tissue from apparently healthy donors. We report a case of a 49-year-old liver transplant patient who presented with metastatic melanoma 9 months after transplantation for hepatocellular carcinoma and who later succumbed to the disease. To investigate the possibility that melanoma was derived from the donor liver, we used a commercially available polymerase chain reaction-based microsatellite marker assay to perform tissue identity testing. The genetic profiles of the patient's original hepatocellular carcinoma and the melanoma from the autopsy specimen were compared with the profile of the normal donor liver tissue, which was still available for testing. The pattern of microsatellite allelic expression strongly suggested that the melanoma detected at autopsy originated from the transplanted liver.

Carlin, A.M., D.S. Rao, A.M. Meslemani, J.A. Genaw, N.J. Parikh, S. Levy, A. Bhan, and G.B. Talpos. (2006). "Prevalence of vitamin D depletion among morbidly obese patients seeking gastric bypass surgery." *Surg Obesity Related Dis* 2:98-103. **[PDF Full-Text](#)**

Background: Abnormalities in calcium and vitamin D metabolism have been reported after bariatric surgery. The purpose of this study was to evaluate vitamin D nutritional status among morbidly obese patients before gastric bypass surgery. **Methods:** We prospectively studied 279 morbidly obese patients seeking gastric bypass surgery for vitamin D nutritional status as assessed by serum 25-hydroxyvitamin D level. In addition, serum samples were analyzed for calcium alkaline phosphatase (AP), intact parathyroid hormone (PTH), and 1,25-dihydroxyvitamin D. **Results:** Mean patient age was 43 ± 9 years; 87% of the study patients were women, and 72% were white. Serum calcium and AP levels were normal in 88% and 89% of the patients, respectively. Vitamin D depletion, defined as serum 25-hydroxyvitamin D level ≤ 20 ng/mL, was found in 166 patients (60%). An elevated PTH level was found in 48% of the patients. A significant inverse correlation was found between serum 25-hydroxyvitamin D level and both body mass index ($r = .15$; $P = .012$) and serum PTH level ($r = .45$; $P < .001$). Vitamin D depletion was significantly more prevalent in the African-American patients than in the white patients (91% vs. 48%; $P < .001$).

Conclusions: Before gastric bypass surgery, a majority of morbidly obese patients have vitamin D

depletion and secondary hyperparathyroidism. Studies evaluating the effects of gastric bypass on Vitamin D metabolism must consider preoperative vitamin D nutrition status.

Chen, J., A. Zacharek, Y. Li, A. Li, L. Wang, M. Katakowski, C. Roberts, M. Lu, and M. Chopp. (2006). "N-cadherin mediates nitric oxide-induced neurogenesis in young and retired breeder neurospheres." *Neuroscience*. [PDF Full-Text](#)

Neurogenesis may contribute to functional recovery after neural injury. Nitric oxide donors such as DETA-NONOate promote functional recovery after stroke. However, the mechanisms underlying functional improvement have not been ascertained. We therefore investigated the effects of DETA-NONOate on neural progenitor/stem cell neurospheres derived from the subventricular zone from young and retired breeder rat brain. Subventricular zone cells were dissociated from normal young adult male Wistar rats (2-3 months old) and retired breeder rats (14 months old), treated with or without DETA-NONOate. Subventricular zone neurosphere formation, proliferation, telomerase activity, and Neurogenin 1 mRNA expression were significantly decreased and glial fibrillary acidic protein expression was significantly increased in subventricular zone neurospheres from retired breeder rats compared with young rats. Treatment of neurospheres with DETA-NONOate significantly decreased neurosphere formation and telomerase activity, and promoted neuronal differentiation and neurite outgrowth concomitantly with increased N-cadherin and beta-catenin mRNA expression in both young and old neurospheres. DETA-NONOate selectively increased Neurogenin 1 and decreased glial fibrillary acidic protein mRNA expression in retired breeder neurospheres. N-cadherin significantly increased Neurogenin 1 mRNA expression in young and old neurospheres. Anti-N-cadherin reversed DETA-NONOate-induced neurosphere adhesion, neuronal differentiation, neurite outgrowth, and beta-catenin mRNA expression. Our data indicate that age has a potent effect on the characteristics of subventricular zone neurospheres; neurospheres from young rats show significantly higher formation, proliferation and telomerase activity than older neurospheres. In contrast, older neurospheres exhibit significantly increased glial differentiation than young neurospheres. DETA-NONOate promotes neuronal differentiation and neurite outgrowth in both young and older neurospheres. The molecular mechanisms associated with the DETA-NONOate modulation of neurospheres from young and older animals as well as age dependent effects of neurospheres appear to be controlled by N-cadherin and beta-catenin gene expression, which subsequently regulates the neuronal differentiating factor Neurogenin expression in both young and old neural progenitor cells.

Chen, J., A. Zacharek, C. Zhang, H. Jiang, Y. Li, C. Roberts, M. Lu, A. Kapke, and M. Chopp. (2005). "Endothelial nitric oxide synthase regulates brain-derived neurotrophic factor expression and neurogenesis after stroke in mice." *J Neurosci* **25**(9): 2366-75. [PDF Full-Text](#)

Here, we investigate the effects of endothelial nitric oxide synthase (eNOS) on angiogenesis, neurogenesis, neurotrophic factor expression, and neurological functional outcome after stroke. Wild-type and eNOS knock-out (eNOS^{-/-}) mice were subjected to permanent occlusion of the right middle cerebral artery. eNOS^{-/-} mice exhibited more severe neurological functional deficit after stroke than wild-type mice. Decreased subventricular zone (SVZ) progenitor cell proliferation and migration, measured using bromodeoxyuridine, Ki-67, nestin, and doublecortin immunostaining in the ischemic brain, and decreased angiogenesis, as demonstrated by reduced endothelial cell proliferation, vessel perimeter, and vascular density in the ischemic border, were evident in eNOS^{-/-} mice compared with wild-type mice. eNOS-deficient mice also exhibited a reduced response to vascular endothelial growth factor (VEGF)-induced angiogenesis in a corneal assay. ELISAs showed that eNOS^{-/-} mice have decreased brain-derived neurotrophic factor (BDNF) expression but not VEGF and basic fibroblast growth factor in the ischemic brain compared with wild-type mice. In addition, cultured SVZ neurosphere formation, proliferation, telomerase activity, and neurite outgrowth but not cell viability from eNOS^{-/-} mice were significantly reduced compared with wild-type mice. BDNF treatment of SVZ cells derived from eNOS^{-/-} mice restored the decreased neurosphere formation, proliferation, neurite outgrowth, and telomerase activity in cultured eNOS^{-/-} SVZ neurospheres. SVZ explant cell migration also was significantly decreased in eNOS^{-/-} mice compared with wild-type mice. These data indicate that eNOS is not only a downstream mediator for VEGF and angiogenesis but also regulates BDNF expression in the ischemic brain and influences progenitor cell proliferation, neuronal migration, and neurite outgrowth and affects functional recovery after stroke.

Dhar, J. P., L. Essenmacher, J. Ager, and R. J. Sokol. (2006). "Reply." Am J Obstet Gynecol. [PDF Full-Text](#)

Ding, G., Q. Jiang, L. Li, L. Zhang, Z. G. Zhang, S. Panda, J. R. Ewing, and M. Chopp. (2006). "MRI of combination treatment of embolic stroke in rat with rtPA and atorvastatin." J Neurol Sci. [PDF Full-Text](#)

To test the hypothesis that combination treatment of embolic stroke with rtPA and statins improves the efficacy of thrombolytic therapy in rats. Rats subjected to embolic MCA occlusion (MCAo) were randomized into control (n=10) and treatment (n=9) groups. Four hours after MCAo, a combination of rtPA and atorvastatin (treatment) or saline (control) was administered. MRI measurements were performed on all animals at 2 h, 24 h and 48 h after MCAo. The patency of cerebral microvessels was examined using fluorescent microscopy. MRI images showed complete blockage of the right MCA and a reduction of CBF in the territory supplied by the MCA 2 h after MCAo for all animals. By 48 h after stroke, MRI showed that the decreased lesion size, elevated CBF and increased incidence of recanalization were found in treated rats compared with the control rats. The combination treatment significantly increased microvascular patency (16.3+/-5.5% vs. 12.4+/-3.5%, of field-of-view) and reduced the infarct volume (23.1+/-9.6% vs. 38.8+/-13.3%, of hemisphere). These data demonstrate that the co-administration of rtPA and atorvastatin 4 h after ischemia is efficacious and is reflected by the MRI indices of recanalization of the MCA, reduction of secondary microvascular perfusion deficits and reduction of the ischemic lesion.

Ding, G., Q. Jiang, L. Li, L. Zhang, Z. G. Zhang, H. Soltanian-Zadeh, Q. Li, P. A. Whitton, J. R. Ewing, and M. Chopp. (2006). "Characterization of cerebral tissue by MRI map ISODATA in embolic stroke in rat." Brain Res. [PDF Full-Text](#)

ISODATA using MRI parameter-weighted images has been previously employed to characterize ischemic cell damage after stroke in rats. In an effort to increase the objectivity and to further automate the ISODATA, MRI parameter maps were now employed. Male Wistar rats were subjected to embolic stroke and received treatment via a femoral vein at 4 h post-stroke. The control rats received saline and were sacrificed at 6, 24 and 48 h after stroke, respectively. Treated rats received rtPA alone or were treated with a combination of rtPA and an antibody, 7E3 F(ab')(2), against the glycoprotein receptor that binds the platelet to fibrin. These rats were sacrificed at 24, or 48, h post-stroke. T(1), T(2) and diffusion maps were employed for map ISODATA analysis. H&E histological analysis of coronal sections of tissue was performed and compared with map ISODATA from the corresponding sections. ISODATA signatures were highly correlated (R approximately 0.80, P < 0.0001) with the ischemic cell damage analyzed at 6, 24 and 48 h post-stroke. At 24 and 48 h after stroke, ISODATA lesion sizes were highly correlated (R > 0.97, P < 0.001) with lesion sizes measured histologically. The combination treatment of rtPA and 7E3 F(ab')(2) reduced both infarction size (P < 0.002) and average signature (P < 0.03) at 48 h after stroke, compared to saline-treated animals. No significant difference was found between saline and rtPA-alone-treated rats. The map ISODATA successfully provides objective and automated quantitation of the ischemic damage in both size and severity in an embolic stroke model of rat with and without a therapeutic intervention.

Harding, P., L. Balasubramanian, J. Swegan, A. Stevens, and W. F. Glass. (2006). "Transforming growth factor beta regulates cyclooxygenase-2 in glomerular mesangial cells." Kidney Int **69**(9): 1578-85. [PDF Full-Text](#)

This study examines the hypothesis that transforming growth factor beta (TGFbeta) regulates cyclooxygenase-2 (COX-2) and induces prostaglandin E synthase (mPGES-1) in rat mesangial cells. COX-2 expression was determined by Northern blot analysis after treatment with either TGFbeta1 or the selective COX-2 inhibitor, NS398. mPGES-1 expression was determined by real-time polymerase chain reaction. The effect of TGFbeta1 on COX-2 gene transcription was assessed using a luciferase reporter assay, and mRNA stability was also determined. To determine whether TGFbeta1 activates elements of the COX-2 promoter, we performed gel shift analyses to examine activation of activator protein-1 (AP-1) and nuclear factor kappaB (NF-kappaB). Prostaglandin E(2) (PGE(2)) and thromboxane B2 (TxB2) production was assayed by enzyme immunoassay. Finally, the pathophysiological relevance of COX-2 inhibition on

the downstream effects of TGFbeta was assessed by examining collagen type I mRNA and net collagen production. COX-2 mRNA and mPGES-1 were induced after treatment with TGFbeta1 for 4 h, and this rise was accompanied by a three-fold increase in PGE(2) production that could be antagonized by selective inhibition of COX-2 with NS398. TGFbeta1 increased transcription by approximately 50% and activated both AP-1 and NF-kappaB. These effects were antagonized by co-treatment with NS398. Treatment with TGFbeta1 also doubled the half-life of COX-2 mRNA. Neither collagen type I mRNA nor net collagen production were altered by co-treatment with NS398. In conclusion, these results indicate that TGFbeta stimulates COX-2 and mPGES-1, with additional effects on transcription and stability of COX-2

Jin, J. Y., E. E. Klein, F. M. Kong, and Z. Li. (2005). "An improved internal mammary irradiation technique in radiation treatment of locally advanced breast cancers." *J Appl Clin Med Phys* **6**(1): 84-93. **Full-Text Not Available / [Click for Article Request Form](#)**

The purpose of the present study was to compare a new internal mammary irradiation technique with traditional techniques for locally advanced breast cancers in terms of sparing ipsilateral lung and heart and reducing the "cold" and "hot spots" in breast tissue. The new technique uses wide tangential fields for the first eight fractions of treatment. A medial internal mammary field (IMF) of electrons matched with narrowed tangential fields is used for the remaining fractions. Intensity-modulated radiation therapy (IMRT) by means of segmented multileaf collimation (SMLC) is used in the narrowed tangential fields to improve the match between the electron and the photon fields. Treatment planning was performed to compare this technique to a wide-tangential-only technique and to a traditional oblique IMF technique for three patients with differing habitus. Film dosimetry was performed in a solid water phantom to confirm the planning results. For all three patients, the mean doses of the ipsilateral lung and the heart were significantly reduced with the new technique. The lung and the heart volumes were remarkably reduced at lowdose levels (< or =12 Gy) compared to the traditional IMF technique, and significantly reduced at all dose levels compared to the wide tangential technique. The new technique also reduced the "cold" and "hot spots" along the match plane between the IMF and the tangential fields compared to the traditional IMF technique. In conclusion, the new IMF technique shows dosimetric improvement compared to the traditional IMF technique in terms of the critical organ sparing and target dose uniformity.

Kaul, S., A. Savera, K. Badani, M. Fumo, A. Bhandari, and M. Menon. (2006). "Functional outcomes and oncological efficacy of Vattikuti Institute prostatectomy with Veil of Aphrodite nerve-sparing: an analysis of 154 consecutive patients." *BJU Int* **97**(3): 467-72. **[PDF Full-Text](#)**

OBJECTIVES: To report updated results, at 1 year of follow-up, of a modified nerve-sparing robotic radical prostatectomy that preserves the lateral prostatic fascia (Veil of Aphrodite). **PATIENTS AND METHODS:** From January to December 2003, 154 consecutive men had a Vattikuti Institute prostatectomy with Veil of Aphrodite nerve-sparing by one surgeon. A prospective database recorded patient demographics, intraoperative, peri-operative, and pathological variables. Peri-operative complications were recorded using the Clavien classification. Patients had serum prostate-specific antigen (PSA) levels measured every 3 months and self-administered the International Prostate Symptom Score and Sexual Health Inventory for Male questionnaires before and at 1 year after surgery. **RESULTS:** The men had a mean age of 57.4 years, a mean body mass index of 27.2 kg/m(2), and a mean PSA level before surgery of 5.11 ng/mL. The mean operative duration was 122 min. At 1 year, 96% of the men reported having had intercourse and 71% had recovered normal erectile function. One man had a Clavien grade II complication, 4.6% of men with organ-confined disease had positive surgical margins, and no patient had a PSA recurrence at 12 months; 97% of the men were continent at 1 year, and the median time to continence was 14 days. **CONCLUSION:** Veil of Aphrodite nerve-sparing surgery provides better recovery of sexual function at 1 year than in contemporary series from centres of excellence, without compromising cancer control and urinary function.

Keteyian, S. J. (2006). "Revisiting the connection between heart rate response during exercise and morbidity in patients with heart failure." *J Cardiopulm Rehabil* **26**(2): 90-1. **[PDF Full-Text](#)**

Lamerato, L., S. Havstad, S. Gandhi, D. Jones, and D. Nathanson. (2006). "Economic burden associated with breast cancer recurrence: findings from a retrospective analysis of health system data." *Cancer* **106**(9): 1875-82. [PDF Full-Text](#)

BACKGROUND: The economics of breast cancer recurrence are poorly understood. For this retrospective cohort study, the authors evaluated the economic burden of breast cancer recurrence by using data from a large Midwestern healthcare system. **METHODS:** Women with Stage I or II breast cancer (according to the American Joint Commission on Cancer staging criteria) were identified from the tumor registry of the Henry Ford Health System. The economic burden of breast cancer recurrence was estimated from patient charges (adjusted to 2003 U.S. dollars). **RESULTS:** From 1996 to 2002, 1616 patients with early breast cancer were identified, including 192 patients who had recurrent tumors. Patients with recurrence had significantly greater charges in the 6-month and 12-month postrecurrence periods (\$45,855 and \$79,253, respectively) compared with the 6-month and 12-month prerecurrence periods (\$10,715 and \$12,344, respectively; both $P < .001$). This was evident for all recurrence types (locoregional, contralateral breast, and distant), but it was most evident for distant recurrences. In a regression analysis that was adjusted for baseline characteristics, the mean monthly charges were significantly greater for patients with recurrence versus patients without recurrence ($P < .001$), and this was true for each recurrence type. For women with recurrence ($n = 74$ patients), the mean charges during the 6-month postrecurrence period were significantly greater than mean charges during the initial 6-month period after diagnosis (\$50,355 vs. \$38,254; $P < .01$). Quarterly charges for continuing care postrecurrence were significantly greater than prerecurrence charges (\$4934 vs. \$1825; $P < .001$). The mean charges for terminal care were significantly greater ($P < .01$) for women with recurrence ($n = 27$ patients, \$63,434) versus women without recurrence ($n = 65$ patients, \$53,872). **CONCLUSIONS:** Patients with early breast cancer who experienced recurrence required more costly care than patients who did not develop recurrent disease. Therapies that reduce the risk of recurrence may reduce costs significantly. *Cancer* 2006. (c) 2006 American Cancer Society.

Moran, J. E., C. L. Drake, and N. Tepley. (2004). "ICA methods for MEG imaging." *Neurolog Clin Neurophysiol* **2004**: 72. **Full-Text Not Available / [Click for Article Request Form](#)**

Activity of individual cortical sources cannot be uniquely imaged when MEG data is a sequence of complex spatial patterns of multiple cortical sources. Auxiliary constraints integrated into the imaging equations are required to remove the mathematical ambiguity. Therefore, it is important to adapt source separation techniques to MEG imaging. It is much easier to accurately image field patterns of isolated brain electric sources. We demonstrate how a combination of second and fourth order Independent Component Analysis (ICA) methods can be used to remove noise and isolate source activity for improved MEG imaging accuracy. A second order ICA technique was used to extract respiratory and eye movement artifact by exploiting cross-correlation differences over time between cortical sources and artifact. For brain electric source separation, a fourth order ICA technique that quantified probabilities of simultaneous source activity was used to separate brain electric sources characterized by bursts of oscillatory circuit activity.

Movsas, D. B., D. C. Scott, and D. D. Watkins-Bruner. (2006). "Pretreatment factors significantly influence quality of life in cancer patients: A radiation therapy oncology group (RTOG) analysis." *Int J Radiat Oncol Biol Phys.* [PDF Full-Text](#)

PURPOSE: The purpose of this analysis was to assess the impact of pretreatment factors on quality of life (QOL) in cancer patients. **METHODS AND MATERIALS:** Pretreatment QOL (via Functional Assessment of Cancer Therapy [FACT], version 2) was obtained in 1,428 patients in several prospective Radiation Therapy Oncology Group (RTOG) trials including nonmetastatic head-and-neck ($n = 1139$), esophageal ($n = 174$), lung ($n = 51$), rectal ($n = 47$), and prostate ($n = 17$) cancer patients. Clinically meaningful differences between groups were defined as a difference of 1 standard error of measurement (SEM). **RESULTS:** The mean FACT score for all patients was 86 (20.7-112) with SEM of 5.3. Statistically significant differences in QOL were observed based on age, race, Karnofsky Performance Status, marital status, education level, income level, and employment status, but not by gender or primary site. Using the SEM, there were clinically meaningful differences between patients ≤ 50 years vs. ≥ 65 years. Hispanics had worse QOL than whites. FACT increased linearly with higher Karnofsky Performance Status and income levels. Married patients (or live-in relationships) had a better QOL than single, divorced, or widowed patients. College graduates had better QOL than those with less education. **CONCLUSION:** Most

pretreatment factors meaningfully influenced baseline QOL. The potentially devastating impact of a cancer diagnosis, particularly in young and minority patients, must be addressed.

Ortiz, P. A. (2006). "cAMP increases surface expression of NKCC2 in rat thick ascending limbs: role of VAMP." *Am J Physiol Renal Physiol* **290**(3): F608-16. [PDF Full-Text](#)

NaCl absorption by the thick ascending limb of Henle's loop (TAL) is mediated by the apical Na-K-2Cl cotransporter NKCC2. cAMP increases NaCl absorption in the TAL by stimulating NKCC2. In oocytes, cAMP increases NKCC2 activity by regulating its trafficking. However, the mechanism by which cAMP stimulates NKCC2 in TALs is not clear. We hypothesized that cAMP increases surface expression of NKCC2 and NaCl absorption in TALs and that vesicle-associated membrane protein (VAMP) is involved in this mechanism. We used surface biotinylation of rat medullary TALs (mTAL) to examine surface and total NKCC2 levels. When mTAL suspensions were treated with dibutyryl cAMP (db-cAMP) or forskolin plus IBMX for 20 min, surface NKCC2 expression increased by 126 +/- 23 and 92 +/- 17% above basal, respectively (P < 0.03). No changes in total NKCC2 expression were observed, suggesting that cAMP increased translocation of NKCC2. We studied the role of VAMP in NKCC2 translocation and found that incubating mTALs with tetanus toxin (30 nM), which inhibits vesicle trafficking by inactivating VAMP-2 and -3, completely blocked the stimulatory effect of db-cAMP on surface NKCC2 expression (tetanus toxin = 100% vs. tetanus toxin + db-cAMP = 102 +/- 21% of control; not significant). We studied VAMP-2 and -3 expression and localization in isolated perfused TALs by confocal microscopy and found that both of them were located in the subapical space of the TAL. Finally, in isolated perfused mTALs, db-cAMP increased net Cl absorption by 95.0 +/- 34.8% (P < 0.03), and pretreatment of TALs with tetanus toxin blocked the stimulation of Cl absorption (from 110.9 +/- 15.9 to 109.7 +/- 15.6 pmol.min(-1).mm(-1); not significant). We concluded that cAMP increases NKCC2 surface expression by a mechanism involving VAMP and that NKCC2 trafficking to the apical membrane is involved in the stimulation of TAL NaCl absorption by cAMP.

Raab, S. S., C. H. Stone, C. S. Jensen, R. J. Zarbo, F. A. Meier, D. M. Grzybicki, C. M. Vrbin, N. P. Otori, and L. Dahmouh. (2006). "Double slide viewing as a cytology quality improvement initiative." *Am J Clin Pathol* **125**(4): 526-33. [PDF Full-Text](#)

Few studies have measured the effect of pre-sign out double viewing of cytology cases as a means to decrease error. Three Agency for Healthcare Research and Quality-funded project sites performed pre-sign out double viewing of 431 pulmonary cytology cases. Two-step or more differences in diagnosis were arbitrated as interpretive errors, and the effect of double viewing was measured by comparing the frequency of cytologic-histologic correlation-detected errors in the previous 2 years with the double-viewing period. The number of interpretive errors detected by double viewing for the 3 institutions was 2.7%, 0% and 1.9%, respectively. Double viewing did not lower the frequency of cytologic-histologic correlation false-negative errors. We conclude that double viewing detects errors in up to 1 of every 37 cases and that biases in the double-viewing process limit error detection.

Reddy, G. P., E. R. Barrack, Q. P. Dou, M. Menon, R. Pelley, F. H. Sarkar, and S. Sheng. (2006). "Regulatory processes affecting androgen receptor expression, stability, and function: Potential targets to treat hormone-refractory prostate cancer." *J Cell Biochem*. [PDF Full-Text](#)

Prostate cancer cells rely on androgen receptor (AR) for proliferation and survival. Therefore, curing prostate cancer will require elimination of AR. Although androgen is the natural ligand that activates AR, AR activity is also subject to regulation by growth factor/growth factor receptor-stimulated signaling pathways that control the cell cycle. Cell cycle regulatory proteins and protein kinases in signaling pathways affected by growth factors can lead to AR activation in the absence of androgen. While downstream signaling proteins such as cyclins, cyclin-dependent kinases (CDKs), and pRB can modulate AR activity, upstream signaling pathways involving protein kinases such as mitogen-activated protein kinases, protein kinase A, and protein kinase B/Akt can affect post-translational modification of AR to affect not only AR function but also AR stability. Calcium and calmodulin (CaM), essential for proliferation and viability of a number of cells, including prostate cancer cells, play an important role in AR expression, stability, and function. CaM affects AR partly by interacting directly with AR and partly by activating protein kinases such as Akt and DNA-PK that can phosphorylate AR. The ubiquitin/26S

proteasome pathway responsible for timely destruction of cell cycle regulatory proteins whose levels impede cell cycle progression also induces AR expression by activating NF-kappaB, and promotes AR activity by participating in the assembly of an AR transcription complex. Maspin, a serine protease inhibitor that is known mostly for its role as a tumor suppressor can also regulate AR intracellular localization and function by competing with AR for binding to the chaperone protein Hsp90 and co-repressor HDAC1, respectively. This perspective reviews the experimental evidence implicating these diverse cellular processes in AR expression, stability, and/or function, and presents a rationale for disrupting these cellular processes as a viable option for the treatment of both the hormone-sensitive and the hormone-insensitive prostate cancer.

Sabbah, H. N., and W. C. Stanley. (2005). "Metabolic therapy for heart disease: impact of trimetazidine." *Heart Fail Rev* **10**(4): 281-8. **Full-Text Not Available** / [Click for Article Request Form](#)

Savera, A. T., S. Kaul, K. Badani, A. T. Stark, N. L. Shah, and M. Menon. (2006). "Robotic Radical Prostatectomy with the "Veil of Aphrodite" Technique: Histologic Evidence of Enhanced Nerve Sparing." *Eur Urol*. **Full-Text Not Available** / [Click for Article Request Form](#)

OBJECTIVE: We have recently described a modification (Veil of Aphrodite) designed to preserve the lateral prostatic fascia (LPF) during robotic prostatectomy. Here, we histologically compare the Veil of Aphrodite technique (VT) and standard nerve-sparing technique (ST). **METHODS:** Thirty-six consecutive prostatectomies performed by a single surgeon were processed by the whole-mount method. The right and left anterolateral (AL) zones of each prostate were independently evaluated for LPF, plane of excision, capsular incision/margin status, margin clearance, and quantitative analysis of periprostatic nerve bundles using S100 immunostain. **RESULTS:** There were 42 AL zones with ST and 30 with VT. In all 42 ST zones, the plane of excision was outside the prostate and a rim of LPF was present. The mean margin clearance was 1.4mm (0.6-2.8mm) and the mean nerve bundle count was 10 (3-19). Capsular incision and margin status were negative in all 42. For VT, 24 of 30 zones lacked LPF and the plane of excision ran just by the prostatic edge. The mean margin clearance was 0.3mm (0-1.7mm) and the mean nerve bundle count was two (0-11). Two VT AL zones revealed capsular incision; the margin was negative for tumour in all 30. Differences in the margin clearances and nerve bundle counts between ST and VT were statistically significant ($p < 0.0001$). **CONCLUSIONS:** The LPF contains nerve bundles that run along the surface of the AL zones. The VT is a safe procedure that effectively preserves the LPF and appears to provide enhanced nerve sparing as compared to the ST.

Sharov, V. G., S. Kostin, A. Todor, J. Schaper, and H. N. Sabbah. (2005). "Expression of cytoskeletal, linkage and extracellular proteins in failing dog myocardium." *Heart Fail Rev* **10**(4): 297-303. **Full-Text Not Available** / [Click for Article Request Form](#)

In the setting of chronic heart failure (HF), progressive left ventricular (LV) dysfunction and chamber remodeling may be due, in part, to altered expression and disorganization of cytoskeletal, linkage and extracellular proteins. This brief review describes changes in expression of cytoskeletal, linkage and extracellular protein using LV tissue obtained from dogs with progressive HF produced by multiple sequential intracoronary microembolizations. LV tissue samples from 6 untreated HF dogs (LV ejection fraction 20% to 25%) and 3 normal dogs were used. Sections from freshly frozen tissue were prepared, immunostained for specific proteins and studied by confocal microscopy. In failing hearts, confocal microscopy showed disorganization of key cytoskeletal proteins that, when combined with the loss of myofilaments and sarcomeric skeleton, suggest substantial cardiomyocyte remodeling. Cardiomyocytes in areas bordering old infarcts invariably exhibited disorganization of alpha-actinin. The cytoskeleton protein desmin showed increased expression in areas of extensive fibrosis. Staining for pancadherin showed interruptions of intercalated disks in areas of intensive interstitial fibrosis. Observation of increased fibronectin and increased interstitial cellularity based on vimentin labeling is suggestive of ongoing fibrosis. Based on these findings, we conclude that the structural changes observed in failing LV myocardium of dogs with intracoronary microembolizations-induced HF are extensive and typical of those

seen and previously described in LV myocardium of explanted failed human hearts. The observed structural changes in this experimental model of HF also support the notion that these cytoskeletal, linkage and extracellular disorganization of structural proteins may be important maladaptations that contribute, albeit in part, to the progression of LV dysfunction and remodeling characteristic of the HF state.

Sharov, V. G., A. V. Todor, M. Imai, and H. N. Sabbah. (2005). "Inhibition of mitochondrial permeability transition pores by cyclosporine a improves cytochrome C oxidase function and increases rate of ATP synthesis in failing cardiomyocytes." *Heart Fail Rev* **10**(4): 305-10. **Full-Text Not Available** / [Click for Article Request Form](#)

Background: We previously showed that mitochondrial respiratory function is abnormal in dogs with chronic heart failure (HF). Mitochondrial permeability transition pores (MPTP) can affect mitochondrial inner membrane potential ($\Delta\psi$) and mitochondrial function in normal cardiomyocytes. The potential impact of MPTP on $\Delta\psi$ and mitochondrial respiratory function in HF has not yet been determined. We tested the hypothesis that cyclosporine A, a potent blocker of the MPTP, can improve mitochondrial function in HF. Methods: Cardiomyocytes were isolated from the left ventricular myocardium of 7 dogs with HF produced by intracoronary microembolizations and from 7 normal dogs. Cardiomyocytes were treated for 24 hours with cyclosporine A. $\Delta\psi$, cytochrome c oxidase protein expression, mitochondrial cytochrome c oxidase-dependent respiration (CDOR) and ATP synthesis were measured. Results: $\Delta\psi$, protein expression of cytochrome c oxidase, CDOR and the rate of ATP synthesis were decreased in HF compared to normal controls. Inhibition of MPTP in failing cardiomyocytes with low dose of cyclosporine A (0.2 μ M) increased $\Delta\psi$, preserved expression of cytochrome c oxidase, improved CDOR and the rate of ATP synthesis. Conclusion: MPTP opening contributes to the loss of mitochondrial function observed in the failing heart. Inhibition of MPTP opening represents a potential therapeutic target for the treatment of HF.

Shen, L. H., Y. Li, J. Chen, A. Zacharek, Q. Gao, A. Kapke, M. Lu, K. Raginski, P. Vanguri, A. Smith, and M. Chopp. (2006). "Therapeutic benefit of bone marrow stromal cells administered 1 month after stroke." *J Cereb Blood Flow Metab*. **Full-Text Not Available** / [Click for Article Request Form](#)

Bone marrow stromal cells (BMSCs) facilitate functional recovery in rats after stroke when administered acutely (1 day) or subacutely (7 days). In this study, we postponed the time of cell transplantation to 1 month after stroke. Female retired breeder rats were subjected to 2 h of middle cerebral artery occlusion (MCAo). Male BMSCs (3×10^6) or phosphate-buffered saline were administered intravenously, and the animals were killed 3 months later. An additional population of nontreated rats was killed at 1 month after MCAo. Significant recovery of behavior was found in BMSC-treated rats beginning at 1 month after cell injection in the modified neurologic severity score test and the adhesive-removal test compared with control animals ($P < 0.05$). In situ hybridization showed that BMSCs survived and preferentially localized to the ipsilateral hemisphere. Double staining revealed that approximately 13% and 6% Y-chromosome-positive cells expressed the astrocyte marker, glial fibrillary acidic protein, and the neuronal marker, microtubule-associated protein-2, respectively. In addition, BMSC treatment reduced scar thickness, and increased the number of proliferating cells and oligodendrocyte precursor cells along the subventricular zone in the ipsilateral hemisphere. Expression of the chemokine stromal-cell-derived factor-1 (SDF-1) was significantly increased along the ischemic boundary zone compared with the corresponding areas in the contralateral hemisphere at 1 month and 4 months ($P < 0.01$) after stroke. The SDF-1 receptor, CXC-chemokine receptor-4 (CXCR4), was expressed in BMSCs both in vitro and in vivo. Our data show that the time window of BMSC therapy is at least 1 month after stroke; the interaction of SDF-1/CXCR4 may contribute to the trafficking of transplanted BMSCs.

Siddiqui, F., L. A. Kachnic, and B. Movsas. (2006). "Quality-of-life outcomes in oncology." *Hematol Oncol Clin North Am* **20**(1): 165-85. **Full-Text Not Available** / [Click for Article Request Form](#)

QOL outcomes have become an integral component of many clinical oncology trials. Much work has been performed testing the validity and reliability of QOL instruments. The current challenge is to understand

better the clinical relevance of QOL research in oncology. QOL studies should focus on phase III trials with clear hypotheses that can lead to clinically meaningful interventions.

Vazquez, J. A., D. J. Skiest, L. Nieto, R. Northland, I. Sanne, J. Gogate, W. Greaves, and R. Isaacs. (2006). "A multicenter randomized trial evaluating posaconazole versus fluconazole for the treatment of oropharyngeal candidiasis in subjects with HIV/AIDS." *Clin Infect Dis* **42**(8): 1179-86. [PDF Full-Text](#)

BACKGROUND: Oropharyngeal candidiasis is the most common opportunistic infection among persons infected with human immunodeficiency virus (HIV). Use of some agents is hampered by lack of efficacy, emergence of resistance, adverse events, and need for intravenous administration. Posaconazole is an extended-spectrum triazole with potent in vitro activity against *Candida* species, including *Candida albicans*, *Candida glabrata*, and *Candida krusei* (including fluconazole-resistant strains). **METHODS:** This multicenter, randomized, evaluator-blinded study of subjects with HIV infection and oropharyngeal candidiasis compared efficacy of posaconazole with that of fluconazole. Subjects received either 200 mg of posaconazole or fluconazole oral suspension on day 1, followed by 100 mg/day for 13 days. The primary study end point--clinical success (cure or improvement) on day 14--was evaluated for 329 subjects. Durability of clinical success was evaluated on day 42. **RESULTS:** Three hundred fifty subjects received posaconazole (n = 178) or fluconazole (n = 172). Clinical success occurred in 155 (91.7%) of 169 posaconazole recipients and in 148 (92.5%) of 160 fluconazole recipients (95% confidence interval, -6.61% to 5.04%), indicating that posaconazole was not inferior to fluconazole. On day 14, mycological success was 68% in both arms, but by day 42, significantly more posaconazole recipients than fluconazole recipients continued to have mycological success (40.6% vs. 26.4%; P=.038). Fewer posaconazole recipients than fluconazole recipients experienced clinical relapse (31.5% vs. 38.2%). Adverse events were similar between treatment arms. **CONCLUSIONS:** Results demonstrate that posaconazole was as effective as fluconazole in producing a successful clinical outcome. However, posaconazole was more effective in sustaining clinical success after treatment was stopped.

Watson, P. Y., A. K. Khandelwal, J. L. Musial, and J. D. Buckley. (2005). "Resident and faculty perceptions of conflict of interest in medical education." *J Gen Intern Med* **20**(4): 357-9. [PDF Full-Text](#)

OBJECTIVE: To determine resident and faculty perceptions of the pharmaceutical industry's influence on medical education. **DESIGN, SETTING, AND PARTICIPANTS:** Anonymous survey of categorical residents and faculty in the department of medicine at a large, Midwestern, urban, independent academic medical center. **MAIN RESULTS:** Eighty-one residents (69.2%) and 196 faculty (75.7%) responded to the survey. Residents believed that a significantly higher percentage of primary care and subspecialist faculty receives industry income or gifts compared to faculty respondents. Many faculty, and to a significantly greater degree residents, indicated that income or gifts influence the teaching of both internal attending physicians and visiting faculty in a variety of educational settings. The majority of residents (61.7%) and faculty (62.2%) believed that annual income or gifts less than \$10,000 could influence an attending physician's teaching. Most residents (65.4%) and faculty (74%) preferred that lecturers report all financial relationships with industry regardless of which relationships the lecturer believes are relevant. **CONCLUSIONS:** Most internal medicine residents and their faculty perceive that industry influences teaching in different educational settings, and want teachers to disclose all of their financial relationships with industry. This information may guide further development of policies and curricula addressing industry relationships within graduate medical education.

Weaver, M., J. Liu, D. Pimentel, D. J. Reddy, P. Harding, E. L. Peterson, and P. J. Pagano. (2006). "Adventitial delivery of dominant-negative p67phox attenuates neointimal hyperplasia of the rat carotid artery." *Am J Physiol Heart Circ Physiol* **290**(5): H1933-41. [PDF Full-Text](#)

Several essential components of NADPH oxidase, including p22(phox), gp91(phox) (nox2) and its homologs nox1 and nox4, p47(phox), p67(phox), and rac1, are present in the vasculature. We previously reported that p67(phox) is essential for adventitial fibroblast NADPH oxidase O(2)(-) production. Thus we postulated that inhibition of adventitial p67(phox) activity would attenuate angioplasty-induced

hyperplasia. To test this hypothesis, we treated the adventitia of carotid arteries with a control adenovirus (Ad-control), a virus expressing dominant-negative p67(phox) (Ad-p67dn), or a virus expressing a competitive peptide (gp91ds) targeting the p47(phox)-gp91(phox) interaction (Ad-gp91ds). Common carotid arteries (CCAs) from male Sprague-Dawley rats were transfected with Ad-control, Ad-p67dn, or Ad-gp91ds in pluronic gel. After 2 days, a 2-F (Fogarty) catheter was used to injure CCAs in vivo. After 14 days, CCAs were perfusion-fixed and analyzed. In 13 experiments, digital morphometry suggested a reduction of neointimal hyperplasia with Ad-p67dn compared with Ad-control; however, the reduction did not reach statistical significance ($P = 0.058$). In contrast, a significant reduction was achieved with Ad-gp91ds ($P = 0.006$). No changes in medial area or remodeling were observed with either treatment. Moreover, adventitial fibroblast proliferation in vitro was inhibited by Ad-gp91ds but not by Ad-p67dn, despite confirmation that Ad-p67dn inhibits NADPH oxidase in fibroblasts. These data appear to suggest that a multicomponent vascular NADPH oxidase plays a role in neointimal hyperplasia. However, inhibition of p47(phox) may be more effective than inhibition of p67(phox) at attenuating neointimal growth.

Wei, S., G. L. Feldman, and K. G. Monaghan. (2006). "Cystic Fibrosis testing among Arab-Americans." *Genet Med* 8(4): 255-8. [PDF Full-Text](#)

PURPOSE: Limited data regarding the cystic fibrosis carrier frequency and mutation detection rate is available for Arab-Americans. We retrospectively determined the frequency of carriers among Arab-Americans undergoing preconception and prenatal carrier screening in our laboratories. METHODS: Between October, 2001 and June, 2005, we performed carrier screening on 805 Arab-Americans, testing for at least the original 25 mutations recommended by the American College of Medical Genetics. We compared our results to previously published studies among Arabic cystic fibrosis patients. We also performed diagnostic testing on seven individuals. RESULTS: Seven carriers were identified, with an observed carrier frequency of 1 in 115. The most common mutation we identified was W1282X (57% of the mutations detected), followed by DeltaF508 and R117H. Three of 7 patients with a known or suspected diagnosis had two identifiable mutations, including 1548delG, DeltaF508, W1282X, 2789 + 5G>A and R170H. CONCLUSION: The current recommended carrier screening panel includes only six mutations reported among Arabic cystic fibrosis patients, accounting for 37.1% of the mutations identified among this group. The addition of 1548delG, I1234V, H139L and 4010del4 as part of an extended screening panel would increase the detection rate to 66.3%, similar to the mutation detection rates in other races/ethnic groups.

Wira, C., G. Martin, J. Stoner, K. Margolis, and M. Donnino. (2006). "Application of normothermic cardiac arrest algorithms to hypothermic cardiac arrest in a canine model." *Resuscitation*. **Full-Text Not Available / [Click for Article Request Form](#)**

BACKGROUND: International guidelines (2000) do not recommend vasopressor and antiarrhythmic medications during ventricular fibrillation (VF) with a core temperature below 30 degrees C. The efficacy of normothermic AHA algorithms using standard doses of epinephrine (EPI) (adrenaline) followed by amiodarone (AMIO) in hypothermic VF is uncertain. OBJECTIVES: To determine the effects of EPI followed by the combination of EPI/AMIO in the treatment of VF in a canine model of severe hypothermia. METHODS: An un-blinded, placebo controlled experiment using 21 mechanically ventilated dogs. Coronary perfusion pressure (CPP), temperature, and electrocardiogram (ECG) were monitored. Animals were cooled to 22 degrees C or the onset of spontaneous VF. VF was induced if necessary. Animals in the treatment group received EPI (0.01mg/kg IV) and defibrillation. This was followed by EPI (0.01mg/kg IV), AMIO (10mg/kg IV) and defibrillation if there was no sustained return of spontaneous circulation (ROSC) for 15min. RESULTS: Mean CPP in the treatment group increased after the administration of EPI/AMIO (24.7+/-13.3mmHg to 46.6+/-7.7mmHg, $p < 0.004$). Cumulatively, the administration of EPI followed by EPI/AMIO achieved ROSC after defibrillation in 10 of 11 animals compared to 3 of 10 in the control group (91% versus 30%, $n=21$, $p=0.0075$). CONCLUSIONS: In this model of severe hypothermia, the use of standard 2000 protocols for VF resulted in a significant increase of CPP, and, a higher ROSC rate compared to placebo controls. This study suggests that AHA normothermic algorithms may be beneficial in severe hypothermia.

Worsham, M. J., K. M. Chen, N. Tiwari, G. Pals, J. P. Schouten, S. Sethi, and M. S. Benninger. (2006). "Fine-mapping loss of gene architecture at the CDKN2B (p15INK4b), CDKN2A (p14ARF, p16INK4a), and MTAP genes in head and neck squamous cell carcinoma." Arch Otolaryngol Head Neck Surg **132**(4): 409-15. [PDF Full-Text](#)

OBJECTIVE: To identify the extent and the smallest region of loss for CDKN2B(INK4b), CDKN2A(ARF,INK4a), and MTAP. Homozygous deletions of human chromosome 9p21 occur frequently in malignant cell lines and are common in squamous cell carcinoma of the head and neck (HNSCC). This complex region encodes the tumor suppressor genes cyclin-dependent kinase 2B (CDKN2B) (p15(INK4b)) and CDKN2A (p14(ARF), p16(INK4a)) and the housekeeping gene methylthioadenosine phosphorylase (MTAP). **DESIGN:** A targeted probe panel designed to finely map the region of 9p21 loss comprised 3 probes for CDKN2B(INK4b), 7 for CDKN2A(ARF, INK4a), and 3 for MTAP and was interrogated using the multiplex ligation-dependent probe amplification assay (MLPA). The MLPA genomic copy number alterations for CDKN2A were validated using real-time polymerase chain reaction. **SUBJECTS:** Six HNSCC primary (A) and recurrent or metastatic (B) cell lines were examined: UMSCC-11A/11B, UMSCC-17A/17B, and UMSCC-81A/81B. **RESULTS:** Cell line UMSCC-11B retained all 9p loci tested in the region. Cell lines UMSCC-17A/B indicated homozygous deletion of CDKN2A(ARF, INK4a) starting at p16(INK4) exon 1alpha to include exons 2 and 3. Homozygous loss was indicated for CDKN2B(INK4b) and CDKN2A(ARF,INK4a) in UMSCC-11A, and UMSCC-81A. Cell line UMSCC-81B indicated retention of all 9p loci except for exon 1alpha (p16(INK4a)). Selective loss of the 3' end of MTAP was observed in UMSCC-11A. Genomic alterations by fine-mapping MLPA were validated at the DNA level for CDKN2A. **CONCLUSIONS:** We identified exon 1alpha (p16(INK4a)) as the smallest region of loss in the CDKN2A(ARF, INK4a) gene. The frequency and precise loss of CDKN2B(INK4b), CDKN2A(ARF, INK4a), and MTAP in the prognosis of 9p21-deleted HNSCC may provide impetus for use of these targets as therapeutic biomarkers in head and neck cancer.

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