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

Anh, D., B. Dudar and K. Ananthasubramaniam (2006). "Acquired isolated left pulmonary vein stenosis: a complication of bronchogenic cyst removal diagnosed by transesophageal echocardiography." *Echocardiography* **23**(1): 73-4. **Full-Text Not Available** / [Click for Article Request Form](#)

Arbab, A. S., W. Liu and J. A. Frank (2006). "Cellular magnetic resonance imaging: current status and future prospects." *Expert Rev Med Devices* **3**(4): 427-439. **Full-Text Not Available** / [Click for Article Request Form](#)

Cellular magnetic resonance imaging (CMRI) allows for the tracking of the temporal and spatial migration of cells labeled with MR contrast agents within organs and tissues. This rapidly growing area of experimental research has the potential of translating from bench to bedside and may be used in conjunction with cellular therapy clinical trials or in the evaluation of novel drug therapies. Ex vivo labeling of nonphagocytic cells with superparamagnetic iron oxide nanoparticles or paramagnetic contrast agents (i.e., gadolinium or manganese) allows for the detection of single cells or clusters of labeled cells within target tissues using CMRI following either direct implantation or intravenous injection. However, prior to the translation of experimental cell labeling studies to clinical trials, it is essential to perform preclinical evaluation to demonstrate a lack of toxicity, the ability to scale-up labeling using good manufacturing practice and the ability to detect cells by in vivo MRI in relevant model systems.

Assal, C. and P. Y. Watson (2006). "Angioedema as a hypersensitivity reaction to polyethylene glycol oral electrolyte solution." *Gastrointest Endosc* **64**(2): 294-5. [PDF Full-Text](#)

Bey, M. J., R. Zuel, S. K. Brock and S. Tashman (2006). "Validation of a new model-based tracking technique for measuring three-dimensional, in vivo glenohumeral joint kinematics." *J Biomech Eng* **128**(4): 604-9. **Full-Text Not Available** / [Click for Article Request Form](#)

Shoulder motion is complex and significant research efforts have focused on measuring glenohumeral joint motion. Unfortunately, conventional motion measurement techniques are unable to measure glenohumeral joint kinematics during dynamic shoulder motion to clinically significant levels of accuracy. The purpose of this study was to validate the accuracy of a new model-based tracking technique for measuring three-

dimensional, in vivo glenohumeral joint kinematics. We have developed a model-based tracking technique for accurately measuring in vivo joint motion from biplane radiographic images that tracks the position of bones based on their three-dimensional shape and texture. To validate this technique, we implanted tantalum beads into the humerus and scapula of both shoulders from three cadaver specimens and then recorded biplane radiographic images of the shoulder while manually moving each specimen's arm. The position of the humerus and scapula were measured using the model-based tracking system and with a previously validated dynamic radiostereometric analysis (RSA) technique. Accuracy was reported in terms of measurement bias, measurement precision, and overall dynamic accuracy by comparing the model-based tracking results to the dynamic RSA results. The model-based tracking technique produced results that were in excellent agreement with the RSA technique. Measurement bias ranged from -0.126 to 0.199 mm for the scapula and ranged from -0.022 to 0.079 mm for the humerus. Dynamic measurement precision was better than 0.130 mm for the scapula and 0.095 mm for the humerus. Overall dynamic accuracy indicated that rms errors in any one direction were less than 0.385 mm for the scapula and less than 0.374 mm for the humerus. These errors correspond to rotational inaccuracies of approximately 0.25 deg for the scapula and 0.47 deg for the humerus. This new model-based tracking approach represents a non-invasive technique for accurately measuring dynamic glenohumeral joint motion under in vivo conditions. The model-based technique achieves accuracy levels that far surpass all previously reported non-invasive techniques for measuring in vivo glenohumeral joint motion. This technique is supported by a rigorous validation study that provides a realistic simulation of in vivo conditions and we fully expect to achieve these levels of accuracy with in vivo human testing. Future research will use this technique to analyze shoulder motion under a variety of testing conditions and to investigate the effects of conservative and surgical treatment of rotator cuff tears on dynamic joint stability.

Chan, P. S., J. P. Caron and M. W. Orth (2006). "Short-term gene expression changes in cartilage explants stimulated with interleukin beta plus glucosamine and chondroitin sulfate." *J Rheumatol* **33**(7): 1329-40. [PDF Full-Text](#)

OBJECTIVE: To determine the short-term effects of glucosamine (GLN) and chondroitin sulfate (CS) on expression of genes encoding inflammatory mediators and matrix enzymes in bovine cartilage explants stimulated with interleukin 1 (IL-1). **METHODS:** Dose-response experiments were conducted for IL-1, GLN, and CS to select concentrations of each optimized for detecting treatment effects on cartilage explants. Based on the dose-response experiments, treatments included fetal bovine serum (FBS) control, 15 ng/ml IL-1, and 15 ng/ml IL-1 with the addition of 10 microg/ml GLN and 20 microg/ml CS. Media were measured for nitric oxide (NO) and prostaglandin E2 (PGE2) while explants were frozen for RNA extraction at 8, 16, and 24 hours. Gene expression relative to FBS control for inducible NO synthase (iNOS), cyclooxygenase-2 (COX-2), microsomal PGE synthase-1 (mPGEs1), nuclear factor-kB p65 subunit (NF-kB), matrix metalloproteinase (MMP)-3 and 13, aggrecanase (Agg)-1 and 2, and tissue inhibitor of metalloproteinase-3 (TIMP-3) were assessed by quantitative real-time polymerase chain reaction (RT-PCR). In a separate study using incubation of explants with the same treatments for 48 hours, proteoglycan release was measured with dimethylmethylene blue assay and TIMP-3 protein was evaluated with Western blots. **RESULTS:** The GLN and CS combination abrogated IL-1-induced gene expression of iNOS, COX-2, mPGEs1, and NF-kB at all timepoints. NO, PGE2, and proteoglycan release were reduced with the combination. The abundance of stimulated MMP-13, Agg-1, and Agg-2 mRNA was repressed, whereas TIMP-3 was upregulated by the combination at all timepoints. The abundance of TIMP-3 protein was increased by the combination relative to IL-1 at 48 hours. **CONCLUSION:** GLN and CS in combination suppress synthesis and expression of genes encoding inflammatory mediators and proteolytic enzymes while upregulating TIMP-3. This provides a plausible mechanism for the purported mild antiinflammatory and chondroprotective properties of GLN and CS.

Chen, P., G. M. Scicli, M. Guo, J. D. Fenstermacher, D. Dahl, P. A. Edwards and A. Guillermo Scicli (2006). "Role of angiotensin II in retinal leukostasis in the diabetic rat." *Exp Eye Res.* Epub Ahead Of Print. **Full-Text Not Available** / [Click for Article Request Form](#)

To study if the endogenous renin-angiotensin system affects diabetic retinal leukostasis, rats with streptozotocin-induced diabetes were treated with an ACE inhibitor (ramipril), an angiotensin II AT(1) receptor antagonist (losartan) and the Ca channel blocker, (nifedipine). In the diabetic rats, these drug

treatments reduced systolic blood pressure by approximately 16mmHg but did not change blood glucose. After 2weeks, the rats were examined for retinal leukostasis in vivo with a scanning laser ophthalmoscope (SLO). Retinal leukostasis, which was defined as no movement of arrested leukocytes over 2min, was markedly higher in diabetic rats than normal controls ($P<0.01$). Leukostasis was significantly decreased by ramipril and losartan ($P<0.01$ vs. untreated diabetic rats) but was still higher than normal. Retinal leukostasis after nifedipine treatment was not significantly different than in untreated diabetic rats. The same trend was observed when leukostasis was analyzed on retinal flat mounts with concanavalin A and CD45 immunofluorescence; ramipril and losartan treatment, however, decreased leukostasis to values no different than controls. Retinal leukostasis was lowered by nifedipine ($P<0.05$, untreated diabetes vs. nifedipine-treated) but was still higher than in normal, ramipril-, or losartan-treated rats. Assays of gene expression of retinal intercellular adhesion molecule (ICAM-1) by semi-quantitative RT-PCR indicated that ICAM-1 mRNA was increased in diabetic rats but was decreased markedly by treatment with losartan or ramipril, and modestly by nifedipine. In summary, suppressing the activity of the endogenous renin-angiotensin system markedly decreases, perhaps even normalizes, the retinal leukostasis that accompanies type I diabetes in rats. These effects seem to be partly independent of blood pressure and to be associated with a decrease in ICAM-1 gene expression. Angiotensin II may, thus, mediate retinal leukostasis in early diabetes.

Cifuentes, M. E. and P. J. Pagano (2006). "Targeting reactive oxygen species in hypertension." *Curr Opin Nephrol Hypertens* 15(2): 179-86. [PDF Full-Text](#)

PURPOSE OF REVIEW: Hypertension is a major risk factor for vascular diseases such as stroke, myocardial infarction, and renal microvascular disease. The mechanism by which vascular disease develops is complex, and growing evidence suggests that an increase in reactive oxygen species during hypertension is a major contributing factor. NADPH oxidase, the primary source of reactive oxygen species in the cardiovascular system, is a strong candidate for the development of therapeutic agents to ameliorate hypertension and end-organ damage. **RECENT FINDINGS:** Various scavengers and inhibitors of reactive oxygen species have been proposed for use in animal as well as human studies. While many of these agents are effective at lowering tissue reactive oxygen species levels, their specificity is a serious concern. Our laboratory has developed cell-permeant peptidic inhibitors targeting key interactions among the different NAD(P)H oxidase homologues. One of these inhibitors targeting nox2 and p47-phox interaction has proven useful in attenuating target neoplasia and hypertrophy. **SUMMARY:** Strategies aimed at specifically inhibiting NAD(P)H oxidase have proven effective in attenuating cardiovascular oxidative stress. The development of new inhibitors targeting novel oxidase homologues appears to hold significant promise for clarifying the physiologic role of these homologues as well as for the development of new antioxidant therapies.

Dhalla, M. S., U. R. Desai and C. Gandolfo (2006). "Does postoperative near visual acuity predict macular hole closure?" *Ophthalmic Surg Lasers Imaging* 37(3): 244-6. **Full-Text Not Available** / [Click for Article Request Form](#)

To determine whether prone postoperative near visual acuity following macular hole surgery can be used as a reliable indicator of successful hole closure, data from 21 patients undergoing macular hole surgery were collected. Seventeen of the 18 patients with hole closure and all 3 patients with persistent macular holes had a Rosenbaum acuity better than preoperative visual acuity, yielding 94% sensitivity, 0% specificity, 85% positive predictive value, and 0% negative predictive value. Fourteen of the 18 patients with macular hole closure and all 3 patients with persistent macular holes had a Rosenbaum acuity better than 20/40, yielding 78% sensitivity, 0% specificity, 82% positive predictive value, and 0% negative predictive value. Although postoperative near visual acuity can predict macular hole closure with 94% sensitivity, the test is not clinically useful to predict hole closure because of the high surgical success rate of macular hole surgery. The test could be useful in encouraging patients to maintain head prone positioning and alleviate patient anxiety.

Faber, M. D. and J. Yee (2006). "Diagnosis and management of enteric disease and abdominal catastrophe in peritoneal dialysis patients with peritonitis." *Adv Chronic Kidney Dis* 13(3): 271-9. **Full-Text Not Available** / [Click for Article Request Form](#)

Peritoneal dialysis (PD)-associated peritonitis rates have decreased significantly in recent years, especially *Staphylococcus epidermidis* and *Staphylococcus aureus* infections. Rates of gram-negative, polymicrobial, and fungal peritonitis have remained steady. The reported mortality of gram-negative and polymicrobial peritonitis varies widely (4%-50%). Most likely, the reason for this variability is that prognosis depends on the underlying etiology more than the specific microorganisms isolated. Gram-negative, polymicrobial, and fungal infection have variable association with documented visceral disease, and the highest mortality occurs in reports with the highest prevalence of intra-abdominal pathology. The odds ratio of death in PD patients with documented abdominal catastrophe and peritonitis is reported to be 20:1 compared with all other causes. Further reductions in PD-associated peritonitis mortality are likely to depend on earlier diagnosis and better management of intra-abdominal pathology. Presentation with hypotension, sepsis, lactic acidosis, and/or elevation of peritoneal fluid amylase should raise immediate concern for "surgical" peritonitis. Suspicion for visceral disease should also be high in patients with gram-negative, polymicrobial, and fungal infection or those who fail to improve rapidly as judged by clinical signs and symptoms, cell counts, and repeat cultures. Nonlocalizing physical examination and negative or nonspecific results of abdominal computed tomography do not rule out serious intra-abdominal disease. Immediate initiation of broad antibiotic coverage including for anaerobic infection is indicated when bowel pathology is suspected. Urgent surgical consultation, with active discussion and participation by the nephrologist, is advisable when visceral pathology is suspected and the patient is unstable or fails to improve rapidly.

Herrera, M., N. J. Hong and J. L. Garvin (2006). "Aquaporin-1 transports NO across cell membranes." *Hypertension* **48**(1): 157-64. [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.

Hong, X., F. Jiang, S. N. Kalkanis, Z. G. Zhang, X. P. Zhang, A. C. DeCarvalho, M. Katakowski, K. Bobbitt, T. Mikkelsen and M. Chopp (2006). "SDF-1 and CXCR4 are up-regulated by VEGF and contribute to glioma cell invasion." *Cancer Lett* **236**(1): 39-45. **Full-Text Not Available** / [Click for Article Request Form](#)

Glioma cells produce vascular endothelial growth factor (VEGF) to induce vascularization and thereby supply the malignant tissue with oxygen and nutrients. However, little is known about the direct effects of VEGF on tumor cells. In this study, we investigate the ability of VEGF to promote proliferation and invasion of human glioma cells (U251n). Since the chemokine and its receptor, SDF-1/CXCR4, promote glioma cell proliferation and are up-regulated in human glioblastomas, we also tested the effects of VEGF on SDF-1 and CXCR4 mRNA expression. Using cell culture, the effect of VEGF on proliferation of U251n cells was measured using ELISA to detect incorporated BrdU as a marker of DNA syntheses. The effects of VEGF and SDF-1 on U251n cell invasion and proliferation were measured using inhibitors to VEGF receptor1 and receptor2, DC101 and MF1, respectively, and a CXCR4 antagonist (AMD3100). SDF-1 and CXCR4 mRNA expression in U251n and U87MG cells were measured using quantitative PCR. VEGF antisense phosphorothioate oligodeoxynucleotide (AS-VEGF) was also used to down-regulate VEGF expression in U251n cells. VEGF significantly increased U251n cell proliferation and invasion in a dose-dependent manner. These effects were blocked by the VEGF receptor inhibitors, DC101/MF1. The CXCR4 antagonist AMD3100 blocked U251n increased invasion, but not proliferation. CXCR4 and SDF-1 mRNA

were up-regulated when U251n and U87MG cells were treated with VEGF. Eight micrometer VEGF antisense phosphorothioate oligodeoxynucleotide (AS-VEGF) down-regulated CXCR4 and SDF-1 mRNA levels in U251n cells. VEGF has a direct effect on U251n glioma cell proliferation and invasion. VEGF up-regulates SDF-1 and CXCR4 mRNA expression, and contributes to U251n cell invasion.

Hudson, M. P. (2006). "Abciximab reduced death, MI, and urgent target vessel revascularization in non-ST-segment elevation acute coronary syndromes." *ACP J Club* **145**(1): 8. [PDF Full-Text](#)

Hudson, M. P., P. W. Armstrong, W. Ruzyllo, J. Brum, L. Cusmano, P. Krzeski, R. Lyon, M. Quinones, P. Theroux, D. Sydłowski, H. E. Kim, M. J. Garcia, W. A. Jaber and W. D. Weaver (2006). "Effects of selective matrix metalloproteinase inhibitor (PG-116800) to prevent ventricular remodeling after myocardial infarction: results of the PREMIER (Prevention of Myocardial Infarction Early Remodeling) trial." *J Am Coll Cardiol* **48**(1): 15-20. [PDF Full-Text](#)

OBJECTIVES: We sought to determine whether matrix metalloproteinase (MMP) inhibitor, PG-116800, reduced left ventricular (LV) remodeling after myocardial infarction (MI). **BACKGROUND:** PG-116800 is an oral MMP inhibitor with significant antiremodeling effects in animal models of MI and ischemic heart failure. **METHODS:** In an international, randomized, double-blind, placebo-controlled study, 253 patients with first ST-segment elevation MI and ejection fraction between 15% and 40% were enrolled 48 \pm 24 h after MI and treated with placebo or PG-116800 for 90 days. Major efficacy end points were changes in LV volumes as determined by serial echocardiography, and clinical and safety outcomes were also collected. **RESULTS:** In total, 203 patients (80%) completed 90 days of treatment and had evaluable baseline and 90-day echocardiograms. The proportion of patients with anterior MI (78% vs. 81%) and primary percutaneous coronary intervention (90% vs. 91%) along with baseline LV ejection fraction (35.5% vs. 36.8%) did not differ between PG-116800-treated and placebo-treated patients. There was no difference in the change in LV end-diastolic volume index from days 0 to 90 with PG-116800 versus placebo (5.09 \pm 1.45 ml/m²) vs. 5.48 \pm 1.41 ml/m², $p = 0.42$). Changes in LV diastolic volume, LV systolic volume, LV ejection fraction, sphericity index, plus rates of death or reinfarction were not significantly improved with PG-116800. PG-116800 was well tolerated; however, there was increased incidence of arthralgia and joint stiffness without significant increase in overall musculoskeletal adverse events (21% vs. 15%, $p = 0.33$). **CONCLUSIONS:** Matrix metalloproteinase inhibition with PG-116800 failed to reduce LV remodeling or improve clinical outcomes after MI.

Jiang, Q., Z. G. Zhang, G. L. Ding, B. Silver, L. Zhang, H. Meng, M. Lu, D. S. Pourabdillah-Nejed, L. Wang, S. Savant-Bhonsale, L. Li, H. Bagher-Ebadian, J. Hu, A. S. Arbab, P. Vanguri, J. R. Ewing, K. A. Ledbetter and M. Chopp (2006). "MRI detects white matter reorganization after neural progenitor cell treatment of stroke." *Neuroimage*. Epub Ahead Of Print. **Full-Text Not Available / [Click for Article Request Form](#)**

We evaluated the effects of neural progenitor cell treatment of stroke on white matter reorganization using MRI. Male Wistar rats ($n = 26$) were subjected to 3 h of middle cerebral artery occlusion and were treated with neural progenitor cells ($n = 17$) or without treatment ($n = 9$) and were sacrificed at 5-7 weeks thereafter. MRI measurements revealed that grafted neural progenitor cells selectively migrated towards the ischemic boundary regions. White matter reorganization, confirmed histologically, was coincident with increases of fractional anisotropy (FA, $P < 0.01$) after stroke in the ischemic recovery regions compared to that in the ischemic core region in both treated and control groups. Immunoreactive staining showed axonal projections emanating from neurons and extruding from the corpus callosum into the ipsilateral striatum bounding the lesion areas after stroke. Fiber tracking (FT) maps derived from diffusion tensor imaging revealed similar orientation patterns to the immunohistological results. Complementary measurements in stroke patients indicated that FT maps exhibit an overall orientation parallel to the lesion boundary. Our data demonstrate that FA and FT identify and characterize cerebral tissue undergoing white matter reorganization after stroke and treatment with neural progenitor cells.

Jiao, Z., Z. G. Zhang, T. J. Hornyak, A. Hozeska, R. L. Zhang, Y. Wang, L. Wang, C. Roberts, F. M. Strickland and M. Chopp (2006). "Dopachrome tautomerase (Dct) regulates neural progenitor cell proliferation." *Dev Biol.* Epub Ahead Of Print. **Full-Text Not Available / [Click for Article Request Form](#)**

DOPachrome tautomerase (Dct) functions downstream of tyrosinase in the biosynthetic pathway of eumelanin by catalyzing the conversion of dopachrome to 5,5-dihydroxyindole-2-carboxylic acid (DHICA) in pigment cells. Dct transcription is regulated directly or synergistically by Pax3, Sox10 and microphthalmia transcription factor (MITF). Using Dct-lacZ transgenic mice, we measured the spatial and temporal pattern of Dct expression in vivo during neocortical neurogenesis in the brain. Dct was expressed in all layers of the dorsal telencephalon in E10.5. At E15.5 and E17.5 when cortical neurogenesis occurs, expression of Dct was primarily localized to the ventricular zone (VZ) where neuronal stem cells reside. Blocking endogenous Dct by RNAi decreased proliferation of embryonic cortical neural progenitor cells (by 48%, $P < 0.05$), as determined by BrdU incorporation. In adult brain, Dct/Dct expression decreased in the subventricular zone (SVZ), dentate gyrus and olfactory bulb (OB). However, strong expression of Dct was observed in rostral migratory stream (RMS) and septum. Overexpression of Dct in SVZ cells derived from the adult mice significantly increased the number of cells by 260%, whereas silencing Dct by RNAi decreased cell numbers by 25.8% at 48 h post-nucleofection ($P < 0.05$). The results of RT-PCR analysis revealed that Dct in the brain lacks exon 7 and is identical to the form of Dct found in neural-crest-derived melanocytes. Our data indicate that Dct, previously known as a melanoblast marker, regulates neural progenitor cell proliferation.

Joseph, C. L., S. Havstad, C. C. Johnson, R. Vinuya and D. R. Ownby (2006). "Agreement between teenager and caregiver responses to questions about teenager's asthma." *J Asthma* **43**(2): 119-24. **[PDF Full-Text](#)**

It is unknown if teenagers and caregivers give similar responses when interviewed about the teen's asthma. We analyzed data for 63 urban African-American teen-caregiver pairs. Caregivers underestimated teen smoking by 30%, gave lower estimates for teen exposure to passive smoke, and disagreed with teens on controller medication usage. Teen-caregiver responses were not significantly different for estimates of symptom-days, activity limitations, or nights awakened; nor were they significantly different for report of emergency department visits or hospitalizations. Agreement was weak for perceived asthma control and severity. Teen-caregiver agreement on asthma depends on the type of information being sought.

Kaul, S., R. Laungani, R. Sarle, H. Stricker, J. Peabody, R. Littleton and M. Menon (2006). "Da Vinci-Assisted Robotic Partial Nephrectomy: Technique and Results at a Mean of 15 Months of Follow-Up." *Eur Urol.* Epub Ahead Of Print. **Full-Text Not Available / [Click for Article Request Form](#)**

OBJECTIVE: Laparoscopic partial nephrectomy is gaining acceptance as an alternative to open surgery for small renal tumours, although technical difficulty of intracorporeal suturing and concerns over warm ischemia time are limitations. Previous work has demonstrated that suturing with the robotic system is easier compared with laparoscopy. We believe the robot has an application and we report our initial experience in 10 patients undergoing robotic partial nephrectomy. **METHODS:** Ten patients with small exophytic renal masses underwent intraperitoneal robotic partial nephrectomy. Principles of traditional open surgery were followed and intraoperative ultrasound was used to define resection margins. The renal artery was clamped with laparoscopic bulldog clamps and indigo carmine was administered intravenously to detect entry into collecting system. Suture closure and FLOSEAL were used for hemostasis. Frozen sections were obtained in all patients. **RESULTS:** Seven men and three women, mean age 59 yr, underwent robotic partial nephrectomy. Mean tumour size was 2cm. Mean console and warm ischemia time were 158min and 21min, respectively. The median hospital stay was 1.5 d. Pathology revealed renal cell carcinoma in eight, oncocytoma in one, and lipoma in one. All resection margins were negative. Follow-up ranged from 6 to 28 mo. **CONCLUSIONS:** Robotic partial nephrectomy is a viable alternative to open or laparoscopic partial nephrectomy in carefully selected patients with small renal tumours. The advantages of the robotic system must be weighed against its cost. Further studies will determine if reduction in procedure complexity warrants the expense of such technology.

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): 1143-4. [PDF Full-Text](#)

Kim, D. G., X. N. Dong, T. Cao, K. C. Baker, R. R. Shaffer, D. P. Fyhrie and Y. N. Yeni (2006). "Evaluation of filler materials used for uniform load distribution at boundaries during structural biomechanical testing of whole vertebrae." *J Biomech Eng* **128**(1): 161-5. **Full-Text Not Available** / [Click for Article Request Form](#)

This study was designed to compare the compressive mechanical properties of filler materials, Wood's metal, dental stone, and polymethylmethacrylate (PMMA), which are widely used for performing structural testing of whole vertebrae. The effect of strain rate and specimen size on the mechanical properties of the filler materials was examined using standardized specimens and mechanical testing. Because Wood's metal can be reused after remelting, the effect of remelting on the mechanical properties was tested by comparing them before and after remelting. Finite element (FE) models were built to simulate the effect of filler material size and properties on the stiffness of vertebral body construct in compression. Modulus, yield strain, and yield strength were not different between batches (melt-remelt) of Wood's metal. Strain rate had no effect on the modulus of Wood's metal, however, Young's modulus decreased with increasing strain rate in dental stone whereas increased in PMMA. Both Wood's metal and dental stone were significantly stiffer than PMMA (12.7 +/- 1.8 GPa, 10.4 +/- 3.4 GPa, and 2.9 +/- 0.4 GPa, respectively). PMMA had greater yield strength than Wood's metal (62.9 +/- 8.7 MPa and 26.2 +/- 2.6 MPa). All materials exhibited size-dependent modulus values. The FE results indicated that filler materials, if not accounted for, could cause more than 9% variation in vertebral body stiffness. We conclude that Wood's metal is a superior moldable bonding material for biomechanical testing of whole bones, especially whole vertebrae, compared to the other candidate materials.

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): 534-41. [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, 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)/Ca²⁺-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 (10 nM) induced a marked increase in intracellular [Ca²⁺]_i that was abolished by [Des-His¹, Glu⁹]-glucagon (1 microM), 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 AT₁ receptor blocker losartan (glucagon + losartan: 77±14%; Ang II + losartan: 84±18%; p<0.01 versus glucagon or Ang II) and the AT₂ 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 (1 microM) or PLC with U73122 (1 microM) 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 (1 microM), a selective PI 3-kinase inhibitor, also blocked glucagon- or Ang II-induced ERK 1/2 phosphorylation. These results suggest that AT₁ 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 AT₂ receptors also play a similar role in this response.

Liu, X. S., Z. G. Zhang, L. Zhang, D. C. Morris, A. Kapke, M. Lu and M. Chopp (2006). "Atorvastatin downregulates tissue plasminogen activator-aggravated genes mediating coagulation and vascular permeability in single cerebral endothelial cells captured by laser microdissection." *J Cereb Blood Flow Metab* **26**(6): 787-96. **Full-Text Not Available / [Click for Article Request Form](#)**

The effects of statins on gene expression of cerebral endothelial cells (ECs) in vivo have not been investigated after stroke. We developed a rapid double immunofluorescent staining protocol with antibodies against von Willebrand factor (a marker for endothelium) and glial fibrillary acidic protein (a marker for astrocytes) for laser capture microdissection to isolate single ECs in brain tissue of the rat. Using this protocol in combination with real-time PCR, we found that stroke significantly increased mRNA levels of protease-activated receptor 1 (PAR-1) and tissue factor (TF) in ECs isolated from ischemic cerebral microvessels compared with nonischemic vessels. Treatment of embolic stroke with recombinant human tissue plasminogen activator (rht-PA) 4 h after stroke further elevated PAR-1 mRNA levels nearly 1000-fold in the core and 500-fold in the boundary above the nonstroke group 30 h after stroke, while TF mRNA levels were elevated approximately 10 fold above the nonstroke group. Furthermore, stroke significantly increased matrix metalloproteinase (MMP) 2 and 9 mRNA levels in the ischemic core and boundary regions 6 and 30 h after stroke. Treatment with rht-PA-upregulated MMP2 expression in the ischemic boundary and core. Atorvastatin completely blocked rht-PA upregulation of the above genes, when atorvastatin in combination with rht-PA was administered 4 h after stroke. Monotherapy of atorvastatin 4 h after stroke did not significantly reduce expression of genes examined in the present study. These data provide evidence that atorvastatin reduces exogenous tPA-aggravated cerebral endothelial genes that mediate thrombosis and blood-brain barrier permeability, which could contribute to the beneficial effects of statins on thrombolytic treatment of acute stroke.

Liu, X. S., Z. G. Zhang, R. L. Zhang, S. Gregg, D. C. Morris, Y. Wang and M. Chopp (2006). "Stroke induces gene profile changes associated with neurogenesis and angiogenesis in adult subventricular zone progenitor cells." *J Cereb Blood Flow Metab*. Epub Ahead Of Print. **Full-Text Not Available / [Click for Article Request Form](#)**

Neural progenitor cells in the subventricular zone (SVZ) of the lateral ventricular wall give rise to new neurons throughout rodent life. Ischemic stroke induces angiogenesis and neurogenesis. Using laser capture microdissection (LCM) in combination with microarrays containing approximately 400 known genes associated with stem cells and angiogenesis, we investigated gene profiles of SVZ cells in the adult mouse subjected to middle cerebral artery occlusion. Our data revealed that nonstroke SVZ cells expressed sets of

genes that are important for neural progenitor cell proliferation, differentiation, and migration. In addition, stroke SVZ cells expressed many genes involved in neurogenesis during embryonic development but were not detected in nonstroke SVZ cells. Stroke upregulated genes were verified by real-time reverse transcriptase-polymerase chain reaction and immunostaining. These data indicate that adult SVZ cells recapture embryonic molecular signals after stroke and provide insight into the molecular mechanisms, which regulate the biological function of neural progenitor cells in the SVZ of adult rodent brain under physiological and stroke conditions.

Lu, M., M. Krams, L. Zhang, Z. G. Zhang and M. Chopp (2005). "Assessing combination treatments in acute stroke: preclinical experiences." *Behav Brain Res* 162(2): 165-72. **Full-Text Not Available / [Click for Article Request Form](#)**

BACKGROUND: Acute ischemic stroke is a complex disease. Treatment success may require combining different therapeutic approaches. An obvious treatment combination in acute ischemic stroke is a thrombolytic therapy, adjuvant with a neuroprotective agent to have better stroke recovery. **SUMMARY OF REVIEW:** Complete factorial designs can assess the synergy of combination treatments and distinguish them from super-additive, additive or sub-additive effects. A factorial design, a two-way analysis of variance and a novel graphic technique can detect and illustrate interactions of two treatments, which were used to evaluate combination treatments to extend the therapeutic window for thrombolytic therapy in an embolic stroke model on rats. We hypothesized synergy or additive effects on stroke recovery when combining thrombolytic therapy with either an antagonist to the integrin CD11b/CD18 (UK-279,276) or a glycoprotein IIb/IIIa receptor inhibitor. **CONCLUSIONS:** Factorial designs offer an efficient approach to study synergistic effects of two treatments. Our graphical technique provides a powerful, intuitive and quantitative explanation of joint treatment effects. Combining thrombolytic therapy with a neuroprotectant yielded a super-additive or additive treatment effect for two preclinical experiments designed to extend the thrombolytic therapeutic window for stroke.

Manierski, C. and A. Besarab (2006). "Antimicrobial locks: putting the lock on catheter infections." *Adv Chronic Kidney Dis* 13(3): 245-58. **Full-Text Not Available / [Click for Article Request Form](#)**

Infectious complications resulting from catheter use in the hemodialysis population remain as the significant cause of morbidity and mortality in this patient population. Because conservation of vascular access sites remains a therapeutic mainstay for chronic hemodialysis patients, clinical investigators have evaluated the safety and efficacy of catheter preservation with antimicrobial lock solutions instilled into the lumens of catheters to treat and prevent infectious complications. The recommended treatment of catheter-related bacteremia includes administration of systemic antibiotics with catheter removal. To date, 4 studies in the hemodialysis population have evaluated the use of systemic antibiotics with an antimicrobial lock solution for treatment of catheter-related bacteremias to amplify the success of catheter salvage. The use of antimicrobial lock solutions for the treatment of catheter-related bacteremia has resulted in successful catheter salvage in approximately 69% of patients, with the remainder requiring catheter removal following a lack of clinical improvement after 48 hours. The antimicrobial lock has also been studied as a prophylactic measure to prevent catheter-related bacteremia. Six studies in the hemodialysis population have evaluated the use of an antimicrobial lock for the prevention of catheter-related bacteremia with an overall 64%-100% reduction in the frequency of catheter-related bacteremia. Although the use of antimicrobial lock for prophylaxis has demonstrated efficacy in clinical trials, its long-term consequences, including potential impact on antimicrobial resistance, are unknown. The objectives of this review are to evaluate the current body of evidence espousing the utilization of an antimicrobial lock solution in tunneled cuffed and uncuffed catheters that are utilized during chronic intermittent hemodialysis.

Movsas, B., C. Scott and 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* 65(3): 830-5. **[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.

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 (FEV₁ 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. FEV₁ 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.

Parasuraman, R., J. Yee, V. Karthikeyan and R. del Busto (2006). "Infectious complications in renal transplant recipients." *Adv Chronic Kidney Dis* **13**(3): 280-94. **Full-Text Not Available /**

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Post-kidney transplant infection is the most common life-threatening complication of long-term immunosuppressive therapy. Optimal immunosuppression, in which a balance is maintained between prevention of rejection and avoidance of infection, is the most challenging aspect of posttransplantation care. The study of infectious complications in immunologically compromised recipients is changing rapidly, particularly in the fields of prophylactic and preemptive strategies, molecular diagnostic methods, and antimicrobial agents. In addition, emerging pathogens such as BK polyomavirus and West Nile flavivirus infections and the introduction of newer immunosuppressive agents that constantly change the risk profiles for opportunistic infections has added layers of complexity to this burgeoning field. Although remarkable progress has been made in these disciplines, comprehensive understanding of the clinical manifestations of infections remains limited, and the standardization of prophylaxis, diagnosis, and treatment of most infections is yet inadequately defined. The long-term goal for optimal care of transplant

recipients, with respect to infection, is the prevention and/or early recognition and treatment of infections while avoiding drug-related toxicities.

Peterson, E. L., C. C. Johnson, J. M. Gorell and B. A. Rybicki (2006). *J Neurol Sci*. Epub Ahead Of Print. [PDF Full-Text](#)

Pladevall, M., B. Singal, L. K. Williams, C. Brotons, H. Guyer, J. Sadurni, C. Falces, M. Serrano-Rios, R. Gabriel, J. E. Shaw, P. Z. Zimmet and S. Haffner (2006). "A Single Factor Underlies the Metabolic Syndrome: A Confirmatory Factor Analysis: Response to McCaffery et al." *Diabetes Care* **29**(7): 1720. [PDF Full-Text](#)

Rastogi, S., R. C. Gupta, S. Mishra, H. Morita, E. J. Tanhehco and H. N. Sabbah (2005). "Long-term therapy with the acorn cardiac support device normalizes gene expression of growth factors and gelatinases in dogs with heart failure." *J Heart Lung Transplant* **24**(10): 1619-25. [PDF Full-Text](#)

BACKGROUND: Passive mechanical containment of the failing left ventricle with the Acorn Cardiac Support Device (CSD) was shown to prevent progressive left ventricular dilation in dogs with heart failure and increase left ventricular ejection fraction. To examine possible mechanisms for improved cardiac function with a CSD, we examined the effect of CSD therapy on the mRNA gene expression of vascular endothelial growth factor (VEGF), basic fibroblast growth factor (bFGF), matrix metalloproteinases (MMP) 2 and 9, and tissue inhibitors of metalloproteinases (TIMP) 1 and 2. **METHODS:** Heart failure was produced in 12 dogs by multiple sequential intracoronary microembolizations. Six dogs were implanted with the CSD and 6 served as concurrent controls. Left ventricular tissue from 6 normal dogs was used for comparison. **RESULTS:** Compared with normal dogs, dogs with untreated heart failure showed downregulation of mRNA expression for VEGF and bFGF, whereas upregulation of mRNA expression for MMP-2 and MMP-9 was observed. Normalization of mRNA expression for all these genes was seen after treatment with the CSD. **CONCLUSIONS:** This study shows that preventing left ventricular dilation and myocardial stretch with the CSD promotes normalization of growth factor and MMP gene expression. These results suggest that modulation of gene activity may, in part, contribute to the improvement of left ventricular function observed with CSD therapy.

Rock, J. P., S. Haines, L. Recht, M. Bernstein, R. Sawaya, T. Mikkelsen and J. Loeffler (2000). "Practice parameters for the management of single brain metastasis." *Neurosurg Focus* **9**(6): ecp2. **Full-Text Not Available / [Click for Article Request Form](#)**

OBJECT: In January 1998 the Guidelines and Outcomes Committee of the American Association of Neurological Surgeons (AANS) issued a charge for the development of evidence-based practice parameters focusing on the treatment of patients with single metastasis to the brain. The charge was imposed in response to the significant controversy surrounding questions relating to the optimal management strategies for patients with single brain metastasis. **METHODS:** A team consisting of physicians from the AANS, the American Academy of Neurology, and the American Association of Therapeutic Radiation Oncology convened and the literature was reviewed. Methodically drawing from the best of Class I, II, and III levels of available evidence, authors sought to determine how the literature addressed and disposed of the question of the optimal management for an adult with a known history of cancer and a single metastatic brain lesion. Framing the question in this specific manner allowed researchers to focus directly on treatment issues, without having to consider diagnostic issues. **CONCLUSIONS:** The results of the evidence-based analysis demonstrated that there was insufficient information to establish standards of care. Data from the literature does, however, support a guideline stating that surgical resection accompanied by whole brain radiation therapy is associated with the best survival rate. Additional lower-quality evidence supports an option for management with radiosurgery.

Roth, T., D. White, W. Schmidt-Nowara, K. A. Wesnes, G. Niebler, S. Arora and J. Black (2006). "Effects of armodafinil in the treatment of residual excessive sleepiness associated with obstructive sleep apnea/hypopnea syndrome: a 12-week, multicenter, double-blind, randomized, placebo-controlled study in nCPAP-adherent adults." *Clin Ther* **28**(5): 689-706. **Full-Text Not Available / [Click for Article Request Form](#)**

BACKGROUND: Some patients with obstructive sleep apnea/hypopnea syndrome (OSA/HS) experience excessive sleepiness (ES) that might not resolve with nasal continuous positive airway pressure (nCPAP) treatment. **OBJECTIVE:** The aim of the present study was to assess the efficacy and tolerability of armodafinil 150 or 250 mg QD when used as adjunctive treatment for residual ES associated with OSA/HS in patients who are adherent to nCPAP therapy. **METHODS:** This 12-week, multicenter, double-blind, randomized, placebo-controlled study was conducted at 37 centers in the United States and Canada. Male and female patients aged 18 to 65 years with residual ES associated with OSA/HS were enrolled. Patients were randomly assigned to receive armodafinil 150 or 250 mg or placebo PO QD for 12 weeks. Assessments were conducted at baseline and study weeks 4, 8, and 12 and included the Maintenance of Wakefulness Test (MWT) to determine wakefulness, the Clinical Global Impression of Change (CGI-C) to determine improvement in clinical condition, the Epworth Sleepiness Scale (ESS) to determine patient-estimated wakefulness, the Brief Fatigue Inventory (BFI) to determine global fatigue, and the Cognitive Drug Research computerized assessment battery. To distinguish between earlier and later effects, sleep latencies, assessed using the MWT, were averaged across the first 4 (9 and 11 AM, and 1 and 3 PM) and last 3 (3, 5, and 7 PM) tests. Tolerability assessments included monitoring of adverse events (AEs), clinical laboratory tests, vital sign measurements, and electrocardiography. **RESULTS:** A total of 395 patients were enrolled in the study (armodafinil 150 mg/d, 133; armodafinil 250 mg/d, 131; placebo, 131); 392 received ≥ 1 dose of study drug (armodafinil 150 mg/d, 131; armodafinil 250 mg/d, 131; placebo, 130). The armodafinil and placebo groups were well matched with regard to age (mean [SD], 49.2 [8.9] vs 50.1 [9.4] years), sex (71 vs 69% men), race (84% vs 87% white), and body weight (mean [SD], 110.3 [24.9] vs 111.9 [24.0] kg). At the final visit, the mean (SD) change from baseline in MWT sleep latency across the morning and afternoon was significantly greater in the armodafinil combined group compared with the placebo group (+1.9 [7.3] vs 1.7 [8.6] minutes; $P < 0.001$). Also at the final visit, the proportions of patients who showed at least minimal improvement on the CGI-C, and the mean (SD) changes from baseline in ESS and BFI scores, were significantly greater in the armodafinil group compared with those in the placebo group (72% vs 37%, -5.5 [5.0] vs -3.3 [4.7], and -1.2 [2.2] vs -0.6 [2.0], respectively; $P < 0.001$, $P < 0.001$, and $P < 0.01$, respectively). No significant effects on nighttime sleep, as assessed using polysomnography, were found with armodafinil. AEs reported in the armodafinil combined and placebo groups were headache, nausea, insomnia, anxiety, and dizziness. Serious AEs (ulcerative colitis, migraine, worsening of Axis II and mood disorder, and duodenal ulcer) were reported in 4 (1.5%) patients receiving armodafinil and were considered by the investigator not or unlikely to be drug related. **CONCLUSIONS:** In this selected population of patients with OSA/HS and residual ES despite effective treatment with nCPAP, armodafinil QD used as an adjunct to nCPAP treatment was associated with improved wakefulness and overall clinical condition. Clinical benefit was shown at the first assessment and maintained for the 12-week duration of the study. Armodafinil was also associated with significantly reduced interference of ES with daily activities and global fatigue. Armodafinil was well tolerated, with no adverse effect on nighttime sleep or nCPAP use.

Roth, T., K. P. Wright, Jr. and J. Walsh (2006). "Effect of tiagabine on sleep in elderly subjects with primary insomnia: a randomized, double-blind, placebo-controlled study." *Sleep* **29**(3): 335-41. **[PDF Full-Text](#)**

SUBJECT OBJECTIVE: This study further evaluated the effects of tiagabine on sleep in elderly subjects with primary insomnia. **METHODS:** Elderly subjects (aged 65-85 years) meeting DSM-IV-TR criteria for primary insomnia were randomly assigned to receive tiagabine 2, 4, 6, or 8 mg or placebo on 2 consecutive nights. Efficacy was assessed using standard polysomnography and a postsleep questionnaire. Additional assessments included the Assessment of Daily Functioning, Digit Symbol Substitution Test (for residual effects), and visual analog scale (for sleepiness/alertness). **RESULTS:** A total of 207 subjects were randomly assigned to study medication (tiagabine: 2 mg, n = 43; 4 mg, n = 38; 6 mg, n = 45; 8 mg, n = 43; placebo, n = 38). Tiagabine did not significantly effect wake after sleep onset, latency to persistent sleep, or

total sleep time compared with placebo ($P > .05$). Significant increases in Stage 3+4 sleep (i.e., slow-wave sleep) were found for tiagabine 4, 6, and 8 mg versus placebo, with a corresponding significant decrease in Stage 1 sleep ($P < .05$). At 6 and 8 mg, tiagabine also significantly reduced the number of awakenings and increased the ratio of Stage 3+4/(Stage 1 +wake after sleep onset). In general, there were no significant effects on subjects' ratings of sleep or daily functioning with tiagabine 2, 4, and 6 mg versus placebo. These 3 doses had tolerability profiles comparable with that of placebo and were not associated with significant residual effects or reduced alertness. The 8-mg dose, however, significantly decreased subjective total sleep time and refreshing quality of sleep, as well as daily functioning. This dose was associated with troublesome adverse events, significant residual effects, and reduced alertness. **CONCLUSIONS:** In elderly subjects with primary insomnia, tiagabine did not have a significant effect on wake after sleep onset, latency to persistent sleep, total sleep time, or the subjective rating of sleep. Tiagabine 4, 6, and 8 mg significantly increased slow-wave sleep, with a corresponding significant decrease in Stage 1 sleep. Tiagabine was generally well tolerated, with doses of less than 6 mg having tolerability profiles generally similar to that of placebo. The 8-mg dose, however, was associated with troublesome adverse events, residual effects, and reduced alertness.

Shah, V. S., A. Ananth, G. K. Sohal, W. Bertges-Yost, A. Eshelman, R. K. Parasuraman and K. K. Venkat (2006). "Quality of life and psychosocial factors in renal transplant recipients."

Transplant Proc **38**(5): 1283-5. [PDF Full-Text](#)

An ideal method for quality of life (QOL) assessment in renal transplant recipients (RTR) has not yet been determined. Present assessments of QOL in RTR are lengthy, cumbersome to administer, and difficult to interpret. We used a previously validated single question QOL scale score (QLS) that directly asks about the patients' overall assessment of their QOL; "Considering all parts of my life-physical, emotional, social, spiritual, and financial--over the past 2 days the quality of my life has been ... ". The QLS ranges from 0 ("very bad") to 10 ("excellent"). Patients were contacted prior to their routine office visit when they were free of acute medical problems. Fifty RTR participated. Psychosocial and medical variables included the Beck Depression Inventory, Illness Effects Questionnaire, Multidimensional Scale of Perceived Social Support, time since transplant, age, creatinine, hemoglobin, and albumin levels. Of the patients, 64% were African-American and 48% were women; 94% of patients had a score >5 . Mean QLS was 7.5 ± 2.3 . Perception of a better QOL correlated with less perception of depression and illness effects and with perception of greater social support and satisfaction with life (all $P < .05$). Perception of QOL did not correlate with age, time since transplantation, creatinine, hemoglobin or albumin levels. We concluded that QLS is a quick tool to measure subjective QOL in RTR for correlation with psychosocial factors of interest in this group. These studies should be replicated in larger multiethnic populations.

Siddiqui, F., C. Y. Li, X. Zhang, S. M. Larue, M. W. Dewhirst, R. L. Ullrich and P. R. Avery (2006). "Characterization of a recombinant adenovirus vector encoding heat-inducible feline interleukin-12 for use in hyperthermia-induced gene-therapy." Int J Hyperthermia **22**(2): 117-34.

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Interleukin-12 (IL-12) is a pro-inflammatory cytokine that has shown great promise as a therapeutic agent in experimental models of infectious disease and cancer. However, it is also a highly toxic molecule and for that reason has not been accepted readily into the clinic. A replication-deficient adenoviral vector was designed to deliver the feline interleukin-12 gene into tumour cells. The interleukin-12 gene has been placed under control of a heat inducible promoter, human heat shock promoter 70b, with the intent of spatially and temporally controlling the expression of IL-12, thus limiting its toxicity. In vitro, the transfection efficiency of the adenoviral vector, the effect of multiplicity of infection and the production of biologically active feline IL-12 were studied in the infected cells in response to a range of temperatures. This adenoviral vector will be a useful tool to examine the effects of intra-tumoural IL-12 delivery in a spontaneously occurring feline soft tissue sarcoma model.

Singh, A., R. V. Goering, S. Simjee, S. L. Foley and M. J. Zervos (2006). "Application of molecular techniques to the study of hospital infection." Clin Microbiol Rev **19**(3): 512-30.

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Nosocomial infections are an important source of morbidity and mortality in hospital settings, afflicting an estimated 2 million patients in United States each year. This number represents up to 5% of hospitalized patients and results in an estimated 88,000 deaths and 4.5 billion dollars in excess health care costs. Increasingly, hospital-acquired infections with multidrug-resistant pathogens represent a major problem in patients. Understanding pathogen relatedness is essential for determining the epidemiology of nosocomial infections and aiding in the design of rational pathogen control methods. The role of pathogen typing is to determine whether epidemiologically related isolates are also genetically related. To determine molecular relatedness of isolates for epidemiologic investigation, new technologies based on DNA, or molecular analysis, are methods of choice. These DNA-based molecular methodologies include pulsed-field gel electrophoresis (PFGE), PCR-based typing methods, and multilocus sequence analysis. Establishing clonality of pathogens can aid in the identification of the source (environmental or personnel) of organisms, distinguish infectious from noninfectious strains, and distinguish relapse from reinfection. The integration of molecular typing with conventional hospital epidemiologic surveillance has been proven to be cost-effective due to the associated reduction in the number of nosocomial infections. Cost-effectiveness is maximized through the collaboration of the laboratory, through epidemiologic typing, and the infection control department during epidemiologic investigations.

Tapia, G. and J. Yee (2006). "Biofilm: its relevance in kidney disease." Adv Chronic Kidney Dis **13**(3): 215-24. **Full-Text Not Available / [Click for Article Request Form](#)**

Biofilm/bioslime is a complex, dynamically interactive multicellular community protected within a heterogeneous exopolysaccharide matrix. Its formation results in the genesis or perpetuation of infection, enhancement of inflammation, and tissue damage or death. Industrial financial losses result from biofilm/bioslime formation; however, the consequences in the medical realm are equally devastating. The relation of biofilm to patients with chronic kidney disease is often covert and extends beyond the colonization of hemodialysis circuits and vascular accesses. Urinary tract device- and vascular access-related biofilms may also increase the burden of cardiovascular risk borne by chronic kidney disease patients, synergizing with the chronic inflammatory state already incurred by these individuals. Current anti-infective strategies are aimed at rapidly killing planktonic forms of microorganisms without specifically targeting the sessile forms that perpetuate their planktonic brethren. Future treatments of infections must ultimately target these reservoirs of infection aiming for their complete eradication. Presently, included among these novel weapons of microdestruction are molecular blocking techniques, electrical enhancement of anti-infectives, and bacterial interference. Nonetheless, the best approach against biofilm formation remains the prevention of microbial colonization, which can be largely by sterile handling of patient-related devices, the most well-established biofilm reservoirs.

Worsham, M. J., K. M. Chen, V. Meduri, A. O. Nygren, A. Errami, J. P. Schouten and M. S. Benninger (2006). "Epigenetic events of disease progression in head and neck squamous cell carcinoma." Arch Otolaryngol Head Neck Surg **132**(6): 668-77. **[PDF Full-Text](#)**

OBJECTIVE: To examine the promoter methylation status of the 22 cancer genes and their contribution to disease progression in 6 head and neck squamous cell carcinoma (HNSCC) cell lines. **DESIGN:** A panel of 41 gene probes, designed to interrogate 35 unique genes with known associations to cancer including HNSCC, was interrogated for alterations in gene copy number and aberrant methylation status (22 genes) using the methylation-specific multiplex ligation-dependent probe amplification assay. **SUBJECTS:** Primary (A) and recurrent or metastatic (B) HNSCC cell lines UMSSC-11A/11B, UMSSC-17A/17B, and UMSSC-81A/81B are described. **RESULTS:** Nine genes, TIMP3, APC, KLK10, TP73, CDH13, IGSF4, FHIT, ESR1, and DAPK1, were aberrantly methylated. The most frequently hypermethylated genes were APC and IGSF4, observed in 3 of 6 cell lines, and TP73 and DAPK1, observed in 2 of 6. For KLK10 and IGSF4, TIMP3 and FHIT, and TP73, in UMSSC-11B, UMSSC-17B, and UMSSC-81B, respectively, promoter hypermethylation was a disease progression event, indicating complete abrogation of tumor suppressor function for KLK10, IGSF4, and TIMP3 and gene silencing of 1 of 2 copies of TP73. Hypermethylation of IGSF4, TP73, CDH13, ESR1, DAPK1, and APC were primary events in UMSSC-17A. **CONCLUSIONS:** Gene silencing through promoter hypermethylation was observed in 5 of 6 cell lines and contributed to primary and progressive events in HNSCC. In addition to genetic alterations of

gains and losses, epigenetic events appear to further undermine a destabilized genomic repertoire in HNSCC.

Yeni, Y. N., J. Yerramshetty, O. Akkus, C. Pechey and C. M. Les (2006). "Effect of fixation and embedding on Raman spectroscopic analysis of bone tissue." *Calcif Tissue Int* **78**(6): 363-71.

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Raman spectroscopy provides valuable information on the physicochemical properties of hard tissues. While the technique can analyze tissues in their native state, analysis of fixed, embedded, and sectioned specimens may be necessary on certain occasions. The information on the effects of fixatives and embedding media on Raman spectral properties is limited. We examined the effect of ethanol and glycerol as fixatives and a variety of embedding media (Araldite, Eponate, Technovit, glycol methacrylate, polymethyl methacrylate, and LR white) on Raman spectral properties (mineralization, crystallinity, and carbonation) measured from the cortical bone of mouse humeri. Humeri were fixed in ethanol or glycerol, followed by embedding in one of the media. Nonfixed, freeze-dried, and fixed but not embedded sections were also examined. Periosteal, endosteal, and midosteal regions of the intracortical envelope were analyzed. Raman spectra of fixative solutions and embedding media were also recorded separately in order to examine the specifics of overlap between spectra. We found significant effects of fixation, embedding, and anatomical location on Raman spectral properties. The interference of ethanol with tissue seemed to be relatively less pronounced than that of glycerol. However, there was no single combination of fixation and embedding that left Raman spectral parameters unaltered. We conclude that careful selection of a fixation and embedding combination should be made based on the parameter of interest and the type of tissue. It may be necessary to process multiple samples from the tissue, each using a combination appropriate for the Raman parameter in question.

Yood, M. U., J. E. Lafata, C. Koro, K. E. Wells and M. Pladevall (2006). "Time to pharmacotherapy change in response to elevated HbA(1c) test results." *Curr Med Res Opin* **22**(8): 1567-74. **Full-Text Not Available / [Click for Article Request Form](#)**

OBJECTIVE: This study describes the clinical management of type 2 diabetes among a cohort of patients receiving oral antidiabetic monotherapy. **Study design and setting:** A retrospective study was conducted within an integrated Midwestern health system that included all individuals receiving oral antidiabetic monotherapy during the period June 1, 1999 to November 30, 2002 (n = 9335). Among patients with elevated hemoglobin A(1c) (HbA(1c)) test result(s), Kaplan-Meier estimates of median time until pharmacotherapy change were calculated. **RESULTS:** Among the 8068 patients who had ≥ 1 HbA(1c) measurement during the study period, 21.4% were at goal (i.e. HbA(1c) < 7%). Among patients with at least one elevated test result ($\geq 7\%$), the median time to pharmacotherapy change following an HbA(1c) test result of between 7-10% was just over 1 year (372 days, 95% confidence interval [CI] 358-393 days) and 160 days for patients with HbA(1c) > 10%. Among patients with at least two elevated tests, the median time to pharmacotherapy change was 275 days from the second test result of between 7-10%, and 70 days among patients with a second HbA(1c) > 10%. The median time between HbA(1c) testing was 166 days overall, and 154 days among patients with at least one elevated result. **CONCLUSION:** Despite the known benefits of glycemic control among patients with diabetes, the time between elevated HbA(1c) results and pharmacotherapy change exceeds 12 months for those with HbA(1c) test results between 7-10% and 9 months for those with results over 10%.

Zael, R., Y. N. Yeni, B. K. Bay, X. N. Dong and D. P. Fyhrie (2006). "Comparison of the linear finite element prediction of deformation and strain of human cancellous bone to 3D digital volume correlation measurements." *J Biomech Eng* **128**(1): 1-6. **Full-Text Not Available / [Click for Article Request Form](#)**

The mechanical properties of cancellous bone and the biological response of the tissue to mechanical loading are related to deformation and strain in the trabeculae during function. Due to the small size of trabeculae, their motion is difficult to measure. To avoid the need to measure trabecular motions during loading the finite element method has been used to estimate trabecular level mechanical deformation. This analytical approach has been empirically successful in that the analytical models are solvable and their

results correlate with the macroscopically measured stiffness and strength of bones. The present work is a direct comparison of finite element predictions to measurements of the deformation and strain at near trabecular level. Using the method of digital volume correlation, we measured the deformation and calculated the strain at a resolution approaching the trabecular level for cancellous bone specimens loaded in uniaxial compression. Smoothed results from linearly elastic finite element models of the same mechanical tests were correlated to the empirical three-dimensional (3D) deformation in the direction of loading with a coefficient of determination as high as 97% and a slope of the prediction near one. However, real deformations in the directions perpendicular to the loading direction were not as well predicted by the analytical models. Our results show, that the finite element modeling of the internal deformation and strain in cancellous bone can be accurate in one direction but that this does not ensure accuracy for all deformations and strains.

Zhang, R. L., Z. Zhang, L. Zhang, Y. Wang, C. Zhang and M. Chopp (2006). "Delayed treatment with sildenafil enhances neurogenesis and improves functional recovery in aged rats after focal cerebral ischemia." *J Neurosci Res* **83**(7): 1213-9. [PDF Full-Text](#)

Increasing age decreases the number of new neurons in the dentate gyrus and the subventricular zone (SVZ). Sildenafil, a phosphodiesterase type 5 (PDE5) inhibitor, enhances neurogenesis in young rats. The present study tested the hypothesis that sildenafil augments neurogenesis in aged rats after focal cerebral ischemia. Nonischemic aged (18 months, n = 6) Wistar rats exhibited a significant reduction of actively proliferating and relatively quiescent cells in the SVZ measured by the number of minichromosome maintenance protein-2-positive (MCM-2+) cells, a marker of the proliferating cells, compared with nonischemic young (3-4 months, n = 8) rats. Occlusion of the middle cerebral artery did not increase the number of MCM-2+ cells in the SVZ of aged rats at 3 months after focal ischemia. However, treatment with sildenafil at a dose of 3 mg/kg (n = 8) daily for 7 consecutive days starting 7 days after focal ischemia significantly increased the number of MCM-2+ cells in the SVZ of aged rats compared with aged rats treated with saline (n = 8). Double immunostaining revealed that substantially more Ki67+ cells (a marker of proliferating cells) were doublecortin+ (a marker of migrating neuroblasts) in sildenafil-treated than in saline-treated aged animals. In addition, treatment with sildenafil significantly improved functional recovery compared with saline-treated rats. These data suggest that inhibition of PDE5 activity by sildenafil augments neurogenesis in the SVZ of aged ischemic rats, although these rats have reduced numbers of neural progenitor and stem cells in the SVZ.

Zhang, R. L., Z. G. Zhang, M. Lu, Y. Wang, J. J. Yang and M. Chopp (2006). "Reduction of the cell cycle length by decreasing G1 phase and cell cycle reentry expand neuronal progenitor cells in the subventricular zone of adult rat after stroke." *J Cereb Blood Flow Metab* **26**(6): 857-63.

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A critical determinant of proliferation of progenitor cells is the duration of the cell division cycle. Stroke increases proliferation of progenitor cells in the subventricular zone (SVZ). Using cumulative and single S-phase labeling with 5-bromo-2'-deoxyuridine, we examined cell cycle kinetics of neural progenitor cells in the SVZ after stroke. In nonstroke rats, 20% of the SVZ cell population was proliferating. However, stroke significantly increased dividing cells up to 31% and these cells had a cell cycle length (T(C)) of 15.3 h, significantly ($P < 0.05$) shorter than the 19 h Tc in nonstroke SVZ cells. Few terminal deoxynucleotidyl transferase-mediated biotinylated UTP nick end labeling-positive cells were detected in the SVZ cells of nonstroke and stroke groups, suggesting that the majority of dividing cells in the SVZ do not undergo apoptosis. Cell cycle phase analysis revealed that stroke substantially shortened the length of the G1 phase (9.6 h) compared with the G1 phase of 12.6 h in nonstroke SVZ cells ($P < 0.03$). This reduction in G1 contributes to stroke-induced reduction of T(C) because no significant changes were detected on the length of S, G2 and M phases between two groups. Furthermore, compared with progenitor cells in nonstroke SVZ (10%), a greater proportion (14%) of progenitor cells in stroke SVZ reentered the cell cycle after mitosis ($P < 0.05$). These results show that an increase in proliferating progenitor cells in the SVZ contributes to stroke-induced neurogenesis and this increase is regulated by shortening the length of the cell cycle, decreasing the G1 phase and increasing cell cycle reentry.

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