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ABSTRACTS

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1 ROLE OF FOLLICULAR DENDRITIC CELL-DERIVED NOTCH SIGNAL IN THE SURVIVAL OF DRUG-RESISTANT B LYMPHOMAS

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Background: Non-Hodgkin's lymphoma is the seventh most common cancer in the US. A significant proportion of patients have experienced relapse due to drug resistance. It is known that lymph node microenvironment (follicular dendritic cells; FDC) promotes B lymphoma cell growth.

Objectives: Because we found that Notch signal derived by FDC played an important role in B cell survival and proliferation, we investigated the Notch signal in the survival of chemotherapy drug-resistant B lymphoma cells.

Methods: The expression of the Notch receptor was detected on B lymphoma cell lines by real-time polymerase chain reaction, and expression of Notch ligands was detected by immunohistochemistry staining. B lymphoma cell lines were treated with chemotherapy drugs (vincristine, etc) in the absence or presence of an FDC. Apoptosis was measured by Annexin-V/PI staining and Western blot.

Results: The B lymphoma cell line expressed Notch receptor (Notch1 and Notch2). FDC expressed Notch ligand Jagged-1 and DLL1. Jagged-1 expressing cells significantly enhanced B lymphoma adhesion and survival. FDC rescued B lymphoma cells from apoptosis induced by chemotherapy drugs. Blocking Notch signaling by γ-secretase inhibitor (i.e., DAPT) abrogates chemotherapy drug resistance of B lymphoma cells conferred by FDC.

Conclusions: FDC-derived Notch ligand (Jagged-1) is a key factor for development of drug resistance by rescuing B lymphoma cells from apoptosis induced by chemotherapy. Therefore, blocking Notch signals from FDC in combination with the current therapy might be more effective in preventing relapse.

2 ROLE OF MACROPHAGES IN HUMAN B LYMPHOMA PROGRESSION

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Background: The tumor microenvironment is characterized by a reactive stroma with an abundance of inflammatory mediators and leukocytes, dysregulated vessels, and proteolytic enzymes. Macrophages are usually the most abundant immune population present in the tumor microenvironment and are often correlated with a bad prognosis. The presence of tumor-associated macrophages (TAMø) has been reported to predict patient outcome in B lymphomas.

Objectives: The aim of this study was to determine the phenotype and functional roles of lymphoma-associated macrophages in B lymphoma progression and how their phenotype is achieved by B lymphoma cells.

Methods: Mononuclear cells from the blood of healthy donors were incubated in 6-well plates for 2 hours at 37°C to remove nonadherent cells. The adherent monocytes were incubated for 7 days in medium with M-CSF (50 ng/mL) to become normal macrophages (nMø). Normal macrophages were cultured for an additional 72 hours in B lymphoma cell-conditioned medium to generate TAMø. The expression of cytokines, chemokines, and angiogenesis factors were compared between nMø and TAMø on the protein and mRNA levels using enzyme-linked immunoabsorbent assay and real-time polymerase chain reaction, respectively. In addition, cell surface molecules were examined by fluorescence-activated cell sorting staining.

Results: B lymphoma cells switched co-cultured macrophages to a phenotype similar to that found in B lymphomas. Tumor cells caused dynamic changes in macrophage cytokine, chemokine, proteolytic enzymes, and angiogenic factors to favor B lymphoma progression.

Conclusions: Interactions between tumor cells and macrophages are important in regulating the cancer cytokine/chemokine microenvironment, thus emphasizing the functional roles of TAMø in the control of the growth and survival of lymphoma cells.

3 INTERACTION OF BREAST CANCER WITH FOLLICULAR DENDRITIC CELLS INDUCES THE METASTASIS TO DISTANT ORGANS

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Background: Breast cancer is the second leading cause of cancer death in women in the United States. During the progression of breast cancer, invasive cancer cells metastasize to disparate organs, including lung, liver, bone marrow, and brain. We have previously shown that follicular dendritic cells (FDCs) promote tumor growth by mammary carcinoma cells and that FDC factors are critical for tumor growth and angiogenesis. Although cancer cells are found frequently in regional lymph nodes at diagnosis in the early stage of breast cancer, it is not known whether the lymph node microenvironment is important for the further metastasis to distant organs. We have previously shown that FDCs promote tumor growth by mammary carcinoma cells.

Objectives: To show whether FDCs enhance metastasis in the distant organs in the animal model.

Methods: Human mammary carcinoma cells (MMCA) and an FDC line, HK cells, were implanted subcutaneously into nonobese diabetes/severe combined immunodeficiency mice. Mice bearing the breast cancers formed with FDCs were examined for the presence of metastasis in the lung, liver, bone, and lymph nodes.

Result and Conclusions: FDC/HK cells induced metastatic tumor growth by distinct subtypes of breast cancer. Estrogen receptor positive MCF7 cells showed enhanced metastasis in the lung by FDC/HK cells. Triple-negative MDA MB 231 cells and Her2-positive BT474 cells were metastasized to multiple organs such as lung, liver, and bone. This suggests that lymph node metastasis is important for the treatment of breast cancer as well as prognosis of patients.

4 LYMPH NODE STROMAL CELLS ENHANCE TUMOR FORMATION OF COLON CANCER STEM CELLS ISOLATED FROM PATIENT SPECIMENS

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Background: Colorectal cancer (CRC) is the third most common malignancy and the second most common cause of cancer-related death in the US. Nearly two-thirds of newly diagnosed cases of CRC have lymph node (LN) metastasis, indicating that the microenvironment in the LN may be important for disease progress. It is also believed that CRC contains a small proportion of drug-resistant cancer cells: colon cancer stem cells (CoCSC). These cells may be responsible for cancer recurrence and invasiveness.

Objectives: To evaluate LN stromal effects using colon cancer patient specimens in a unique xenoplant model established for CoCSC tumor formation.

Methods: Colon cancer suspension cells were isolated by enzyme digestion from consented patients. $CD133^+$ CoCSC were purified for subcutaneous primary tumor formation in nonobese diabetic/severe combined immunodeficient (NOD/SCID) mice. A colon cancer cell line from primary tumors was established and tagged with green fluorescent protein for tumor growth measured by whole body live imaging. Immunohistochemical studies were performed to quantify CoCSC and host infiltrating cells in the original tumor as well as xenoplants.

Results: The LN stromal cell line, HK cells, enhanced colon cancer cell tumor formation in NOD/SCID mice. Inhibitors specific to HK cell-derived SDF-1 reduced colon cancer tumor formation *in vivo*. $CD133^+$ CoCSC isolated from patient specimens are more tumorigenic than unseparated bulk tumor cells. $CD133^+$ and SDF-1 receptor CXCR-4-expressing cells are enriched in chemotherapy-resistant colon cancer cells.

Conclusions: Understanding LN stromal effect on CoCSC may present prognostic significances to better predict tumor recurrence and invasiveness as well as implications for developing targeted therapeutic strategies.

5 TUMOR MICROENVIRONMENT MODELS USING ENHANCED GREEN FLUORESCENT PROTEIN (EGFP) EXPRESSING IMMUNODEFICIENT MICE

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Background: Cancer is a leading cause of death worldwide. In 2009, about 1,479,350 new cancer cases were expected to be diagnosed in the US, 22,170 in Louisiana. The tumor microenvironment involves tumor cells as well as resident and infiltrating nonmalignant cells. Nonmalignant cells play important roles in modulating tumor progression. Thus, better *in vivo* models that enable tumor microenvironment studies are necessary.

Objectives: To establish new *in vivo* models to illustrate tumor-host cell interactions during tumor formation.

Methods: Nonobese diabetic/severe combined immunodeficient mice expressing enhanced green fluorescent protein were used to establish *in vivo* models of human cancers. Matrigel plug assays were used to detect host cell infiltration in early stages; subcutaneous tumor injection was used to study tumor-host cell interactions in later stages. Lymphoma cell lines (FLK, Wanyonyi, and Ramos) and a colon cancer cell line (HT-29) were used for tumor formation. A follicular dendritic cell line (HK) was used to enhance tumor formation. Fluorescence-activated cell sorting (FACS) and immunofluorescent microscopy were used to identify host and cancer cells by specific markers. These models provide a system for detailed cellular and molecular analysis of tumor-host cell interactions. Specific subpopulations of host cells, such as tumor associate macrophages, can be identified and quantified by FACS and immunohistochemistry analysis.

Results: HK cells promote tumor cell survival in early stages and tumor formation by enhancing tumor angiogenesis and recruiting host inflammatory cells to tumor site. Inhibitory reagents specific to HK cell-derived molecules reduced tumor angiogenesis, host cell infiltration, and tumor formation.

Conclusions: Identification of key microenvironmental components in tumorigenesis may present prognostic significances and implications in developing targeted therapeutic strategies to improve cancer treatment.

6 LYN INHIBITION INDUCES APOPTOSIS IN CELL LINES DERIVED FROM TUMORS IN KAPOSI SARCOMA-ASSOCIATED HERPES VIRUS K1 TRANSGENIC MICE

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Background: Kaposi sarcoma-associated herpes virus (KSHV) has been associated with all forms of Kaposi sarcoma and with certain lymphoproliferative disorders. The KSHV-encoded K1 is a signaling protein capable of eliciting B cell activation. Previously, we showed that expression of K1 in mice results in the development of plasmablastic lymphomas. The Lyn kinase-mediated signaling pathway was important for the growth of these lymphomas.

Objectives: To gain further insight into the pathogenetic functions of K1, we investigated its role in the development of tumors in various other cell types.

Methods: Approximately 300 K1 transgenic mice were observed for the development of tumors. Tumor cell lines were generated by using the Cancer Cell Isolation Kit (Panomics). Lyn kinase activity, cell viability, and caspase 3/7 activities were analyzed in cells treated with varying doses of the Lyn kinase inhibitor PP2 or its inactive analogue PP3.

Results: Approximately 7% of K1 transgenic mice developed tumors between 14 and 24 months of age. These tumors were characterized as spindle cell sarcomas, hepatocellular carcinomas, and adenocarcinomas. Lyn kinase activity was found to be constitutively high in the tumors and cell lines derived from these tumors. Treatment of tumor cell lines with PP2 but not PP3 inhibited Lyn kinase, cell viability, and enhanced caspase 3/7 activity in a dose-dependent manner.

Conclusions: Our K1 transgenic mice provide a valuable model to test the oncogenic potential of Lyn kinase in a variety of cell types and to develop more effective treatments for malignancies in humans that show significant activation of this Src family kinase.

7 ECFP/ANG II TRANSGENIC MICE DISPLAY RENAL THROMBOTIC MICROANGIOPATHY AND ELEVATED BLOOD PRESSURE

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Background: We have generated transgenic mice that express angiotensin II fused downstream of enhanced cyan fluorescent protein (EFCP), the expression of which is regulated by the mouse metallothionein housekeeping promoter. The fusion protein, which lacks a secretory signal, is retained intracellularly. In previous published tissue culture studies, we have shown this protein to (1) alter intracellular distribution of the AT_1 receptor, (2) stimulate proliferation of vascular smooth muscle cells, and (3) stimulate CREB transcription factor phosphorylation activation.

Results: In the present transgenic mouse study, whole animal imaging (Caliper LS IVIS), reverse transcription-polymerase chain reaction, immunoblot analyses, and fluorescent microscopy of murine embryonic fibroblasts confirmed expression of the fusion protein *in vivo* and *in vitro*. The transgene is expressed in all tissues investigated (including brain, heart, kidney, liver, lung, and testes). Radioimmunoassays of plasma samples obtained from transgenic mice indicate no increase in circulating Ang II over wild-type (wt) levels, consistent with intracellular retention of the transgene product. Hearts and kidneys from homozygous transgenic and corresponding wt littermates were histologically evaluated. Kidney histology showed transgenic abnormalities consistent with thrombotic microangiopathy. Microthrombosis was frequently observed within the glomerular capillaries and small vessels. In addition, radiotelemetry confirmed elevated systolic and diastolic blood pressures in transgenic mice compared to wt littermates. Male transgenic systolic blood pressure was 135 ± 11 mmHg, diastolic was 100.5 ± 8.6 mmHg ($\pm$ SEM). Male wt systolic blood pressure measured at 111.8 ± 4.9 mmHg and diastolic at 89.6 ± 4.4 mmHg. Female transgenic systolic blood pressure averaged 138.2 ± 10.7 mmHg and diastolic at 101.7 ± 7.9 mmHg. Female wt systolic blood pressure was 110.1 ± 5.7 mmHg and diastolic was 85.3 ± 5.6 mmHg. Transgenic males and females demonstrated significantly higher blood pressure than corresponding wt littermates, $n = 8$ for all groups, $p < 0.001$.

Conclusions: In summary, overexpression of an intracellular fluorescent fusion protein of Ang II corresponds to elevated blood pressure and kidney pathology. This transgenic model may be useful to further explore the intracellular renin-angiotensin system and its implication in abnormal cell growth and hypertension.

8 EXPRESSION OF A NATURALLY OCCURRING ANGIOTENSIN AT_1 RECEPTOR CLEAVAGE FRAGMENT IS CORRELATED WITH CASPASE-ACTIVATION AND APOPTOSIS

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Background: We have previously reported that the AT_1 receptor (AT_1R) is cleaved in an angiotensin II ligand-dependent manner with trafficking of the cytoplasmic carboxy-terminal cleavage fragment (CF) to the nucleus and shedding of the extracellular domain.

Methods: In this study, we have isolated the CF and determined size using mass spectrometry and partial sequence using Edman degradation. The average molecular mass is 7645.9 and corresponds to a cleavage site midway through the 7th transmembrane domain (between aromatic residues Tyr-292 and Phe-293). We have further overexpressed the AT_1R CF as a fluorescent fusion protein and monitored its effects in several cell types. CHO-K1, H9c2 cardiomyoblasts, HeLa, and MCF-7 breast adenocarcinoma cells were transfected with AT_1R_{CF}/enhanced yellow fluorescent protein (or corresponding controls: empty plasmid or full-length receptor) and evaluated by three-dimensional deconvolution imaging for expression and trafficking of the fusion proteins.

Results: Expression of the cleavage fragment causes rapid morphological changes (as early as 3 hours posttransfection), which vary depending on the cell type but are all consistent with apoptosis. Nuclear fragmentation, membrane blebbing, nuclear disintegration, and expression of activated caspases (by FLICKA polycaspase assay) and cell-surface phosphatidylserine (by Biovision annexin V staining) are observed. In addition, expression of the CF is associated with visible DNA laddering as early as 24 hours and dramatic laddering by 48 hours in all cell types examined. DNA laddering is the gold-standard assay for apoptosis but generally is useful only if large populations are simultaneously undergoing cell death. The CF is clearly an extremely powerful apoptotic reagent in all cells examined.

Conclusions: These results are consistent with an apoptotic role for the AT_1R CF. The renin-angiotensin system has been associated with apoptosis in several disease processes, including heart failure, glioblastoma, atherosclerosis, and restenosis. Our data are consistent with the hypothesis that cleavage and nuclear trafficking of the receptor fragment may underlie apoptosis in one or more of these pathologies.

9 ANGIOTENSIN TYPE-1A RECEPTOR INTERACTS WITH SUBUNIT 68 OF THE SIGNAL RECOGNITION PARTICLE

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Background: Hypertension is a major risk factor for myocardial infarction, heart failure, and stroke. The renin-angiotensin system (RAS), an important modulator of blood pressure and cardiovascular physiology, plays a critical role in the etiology of hypertension and the pathophysiology of cardiac, renal, and vascular diseases. The octapeptide angiotensin II (Ang II) is the primary effector of the RAS; its vasoactive effects are mediated by the Ang II type 1 receptor (AT_1R). Understanding the mechanisms, physiological significance, and complex interplays of the circulating, tissue, and intracellular RASs is vital to effective drug development. To this end, initial studies were designed to identify proteins that bind to AT_1R and alter its expression or function. Subunit 68 of the signal recognition particle (SRP68) was identified as an AT_1R-interacting protein.

Objectives: To characterize the interaction between AT_1R and SRP68 and explore the functional consequences of this interaction.

Methods: Interactions between SRP68 and wild-type or mutant AT_1R were assayed by yeast two-hybrid analysis. Protein expression was assessed by immunoblotting. AT_1R signaling was monitored by cyclic AMP response element (CRE)-dependent transcription.

Results: The SRP68 binding site of AT_1R was localized to the membrane proximal region (residues 306–320) of the C-terminal tail. Alanine scanning mutagenesis identified residues F309, K310, Y312, F313, and L316 as critical for binding. All mutants were expressed at similar levels. Overexpression of SRP68 in human cultured cells inhibited Ang II-mediated CRE activation by 50%.

Conclusions: SRP68 binds to the C-terminal, membrane proximal region of AT_1R and inhibits its signaling activity.

10 THE BUBBLE GUM MYSTERY: A PARTICIPATIVE LABORATORY EXPERIMENT FOR MIDDLE SCHOOL STUDENTS

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Background: Ochsner's Science, Technology, Academics, and Research (STAR) program was created to stimulate the interest of local high school students—particularly underrepresented minorities—in biomedical science and health care, with the ultimate goal of expanding the pipeline to careers in these fields. This program disseminates scientific knowledge largely through participation in multiple scientific experiments. Studies suggest that such experiences may have an even greater impact on students' interest in science if the modules are administered at an earlier age.

Objectives: To develop and evaluate an age-appropriate, hands-on laboratory module for middle-school students to be administered in a pilot program at Ochsner's student laboratory, the *i*Lab.

Methods: The "Bubble Gum Mystery" is a DNA forensics-themed experimental module from the BIOTECH Project of the University of Arizona. It was adapted for the *i*Lab and expanded to include a short lecture and a DNA trivia contest. The module (approximately 3 hours in length) was administered during the 2009 calendar year to 10 different 7th and 8th grade science classes from three Orleans and three Jefferson Parish schools. At the end of the experiment, students were required to complete a seven-question evaluation form.

Results: Of the six participating schools, two were private. The experimental module was administered to a total of 236 students, 60% of whom were minorities. A total of 223 evaluation forms were collected and tabulated. On a 5-point Likert scale (1 = strongly disagree, 5 = strongly agree), the statements "I had fun doing this experiment" and "I would like to come and do other experiments offered by the iLab" elicited average scores of 4.68 and 4.60, respectively. Importantly, the students did not consider the subject matter or presentation of the module to be beyond their grade level ("The material covered in this lab was too difficult to understand." Score = 1.71). No statistical differences in these responses were observed between Orleans vs. Jefferson, public vs. private, or 7th grade vs. 8th grade students.

Conclusions: The "Bubble Gum Mystery" is an age-appropriate and enjoyable module and one that stimulates middle school students' interest in science.

11 EVALUATION OF THE 2009 SCIENCE, TECHNOLOGY, ACADEMICS, AND RESEARCH SUMMER PROGRAM FOR HIGH SCHOOL STUDENTS

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Background: The Science, Technology, Academics, and Research (STAR) program was created to stimulate the interest of local students, particularly underrepresented minorities, in biomedical science and health care, with the ultimate goal of expanding the pipeline to careers in these fields. In 2009, the program was modified by increasing eligibility to students from seven parish school districts in the greater New Orleans area. Added to the curriculum were new medical rotations and experimental modules to be carried out within the student learning laboratory, the *i*Lab.

Objectives: To evaluate the effect of open enrollment on the composition of the STAR 2009 class and the overall effectiveness of the newly incorporated rotations and experiments.

Methods: Relevant data were collected from the student application forms and surveys completed by the STAR 2009 students (preprogram, postprogram, postexperiment, and weekly surveys).

Results: Ten schools, public and private, were represented in the class of 2009, compared to only six in 2008. Minority student enrollment increased from 50% to 58.3%, but the number of female students decreased from 83% to 75%. The experimental modules were received very favorably by the students. Significant increases were found in the students' rating of their understanding of DNA fingerprinting and polymerase chain reactions. On a five-point Likert scale, 91.6% of the students rated that having participated in the STAR program would help them in their future science classes.

Conclusions: Overall diversity of the 2009 STAR class increased from that of 2008 due to the greater number of minority participants and parish school districts represented. Although classes and rotations were viewed favorably, there was a detectable preference for more interactive and hands-on health care classes.

12 SALT-INDUCED RENAL INJURY: ROLE OF THE TUBULAR RENIN-ANGIOTENSIN SYSTEM AND PREVENTION BY ANGIOTENSIN II RECEPTOR BLOCKADE

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Background: Salt-loading in the spontaneously hypertensive rat (SHR) promotes cardiac structural and functional damage, which is prevented by an angiotensin II receptor blocker (ARB).

Objectives: To examine the effect of salt-loading, with or without simultaneous angiotensin II blockade on the activity of the renin-angiotensin system (RAS) in SHRs.

Methods: Four groups were studied: Group I was given regular rat chow (NS); Group II, NS with an ARB, losartan (30 mg/kg/daily by gavage); Group III, chow with high salt content (8%) (HS); and Group IV, HS diet plus losartan. Respective treatments lasted 4 weeks, and, at the end, blood and tissue samples for the determinations of components of the RAS were collected.

Results: The data demonstrate that in HS rats arterial pressure increased minimally but significantly [from 180 ± 1 mmHg in NS to 193 ± 1* ($p<0.05$) in HS]; losartan did not affect this (192 ± 2 mmHg). However, HS diet increased urinary protein excretion, which losartan ameliorated. Surprisingly, plasma renin activity was unaffected by HS, but plasma angiotensin II concentration increased 3–4 fold (from 22.1 ± 3.5 fmol/mL in NS to 90.2 ± 15.2* in HS) and urinary angiotensinogen excretion (uAGT) increased 10 fold (from 158 ± 27 ng/day in NS to 1566 ± 296 in HS); these changes were partially prevented by losartan. There was no difference in Ang II concentration in heart and kidneys between the groups.

Conclusions: These data support our earlier reports that the RAS may be involved in the adverse cardiovascular and renal effects of salt-loading. Furthermore, the observed increase in uAGT indicates that the stimulation of angiotensin II production from the renal tubules may mediate salt-induced renal damage.

Clinical relevance: Because excessive salt intake is very common in developed countries whereas pathophysiological consequences of salt-overload are not fully appreciated, it is important to better understand the mechanism of salt-related injury.

13 MTORC2 REGULATES ENDOTHELIAL CELL MIGRATION THROUGH MODULATION OF P27^{KIP1} PROTEIN LEVELS

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14 A NOVEL FUSION PROTEIN FOR THE TREATMENT OF POSTMENOPAUSAL OSTEOPOROSIS

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Background: Daily subcutaneous injections of parathyroid hormone (PTH) stimulate bone growth and can be used as a treatment for osteoporosis. We have shown previously that we can prolong the anabolic effect of PTH in normal mice by attaching it to a collagen-binding domain (CBD) that concentrates and retains PTH in the bone. In this study, we tested PTH-CBD in the recognized animal model of postmenopausal osteoporosis, ovarectomized (ovx) female rats.

Methods: Nine-month-old female Sprague Dawley rats (60 ovx and 12 sham controls) (20% difference in bone mass between the two groups) were divided as follows:

1. Ovx vehicle control (vehicle, single dose)
2. PTH [20 μg/kg/d human PTH(1-34) for 14 days]
3. PTH-CBD (320 μg/kg, single dose)
4. PTH-CBD (320 μg/kg/month)
5. CBD (320 μg/kg, single dose)
6. Sham control (no ovx, single injection, vehicle)

Bone mineral density (BMD) was measured monthly, and blood samples were collected before and after injections.

Results: BMD increased significantly (7.3%) in the PTH-treated group after 1 month, declining to 4.9% after 2 months (vs. ovx vehicle control). PTH-CBD groups showed no change in BMD after 1 month but increased to 10.6% with monthly dosing and 3.4% with single dosing after 2 months. CBD administration had no effect on BMD. Serum calcium increased significantly 20 minutes after PTH administration; there was a lesser increase in serum calcium after PTH-CBD administration, which was not statistically significant.

Conclusions: Overall, when compared to PTH, PTH-CBD had a greater effect on BMD, with reduced hypercalcemia and requiring far fewer injections to achieve these results.

15 TREATMENT OF CHEMOTHERAPY-INDUCED ALOPECIA WITH A NOVEL FUSION PROTEIN

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Background: Parathyroid hormone (PTH) agonists and antagonists were fused with a bacterial collagen-binding domain (CBD) derived from clostridium histolyticum collagenase [PTH(1-33)-CBD and PTH(7-33)-CBD, respectively] to provide targeted drug delivery to skin. The effects of these compounds on chemotherapy-induced alopecia after cyclophosphamide (CYP) administration were tested in mice.

Methods: A total of 28, 5-week-old C57BL/6J mice were divided into four groups (vehicle, CYP+vehicle, CYP+PTH(1-33)-CBD and CYP+PTH(7-33)-CBD). Mice were depilated on the back to synchronize the hair follicles. On day 7, normal and CYP vehicle groups received a single injection of 320 μg/kg buffer, while the other two groups received a single injection of 320 ug/kg of PTH(1-33)-CBD or PTH(7-33)-CBD, respectively. On day 9, 150 mg/kg of CYP was administered to all animals except the vehicle mice.

Results: Vehicle mice showed rapid regrowth of back hair. Histological examination showed normal anagen and telogen hair follicles. CYP+vehicle mice showed severe hair loss and decreased hair pigmentation. Histological examination showed dystrophic anagen and catagen hair follicles, which were localized to the dermal layer; no telogen follicles were observed. The CYP-PTH(1-33)-CBD group showed regrowth and repigmentation of hair after chemotherapy, less complete but comparable to the vehicle mice. Histologically, normal, predominantly anagen follicles were seen penetrating the dermal layer. The CYP-PTH(7-33)-CBD group showed rapid hair regrowth initially, with little change observed afterward.

Conclusions: Overall, both agonists and antagonists to PTH modulated hair growth when linked to a CBD, but the agonist compounds produced the most cosmetically acceptable result.

16 A PHASE II CLINICAL TRIAL OF A NOVEL COMBINATORIAL ANTI-TUMOR IMMUNOTHERAPY FOR PATIENTS WITH HIGH-RISK, RESECTED STAGE III AND METASTATIC MELANOMA

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Background: Patients with advanced melanoma have a uniformly poor outcome despite current treatment options. Cancer immunotherapy is designed to selectively activate the host immune system and destroy tumor cells.

Objectives: To test a novel combinatorial immunotherapeutic approach for patients with high-risk, resected stage III, recurrent, refractory or stage IV melanoma.

Methods: A phase II clinical trial combines HyperAcute® melanoma (HAM) vaccine (NewLink Genetics Corp.) with PEG-Intron® (Schering-Plough Corp.). Trial design consists of a 12-week regimen, the first 4 weeks with HAM vaccine alone (intradermally) followed by weeks 5–12 with HAM vaccine + PEG-Intron® (once weekly, subcutaneously at 6 μg/kg). Trial endpoints include correlative studies for observed anti-tumor effect and, secondarily, determination of overall safety and response rates. The planned sample size is 25 patients.

Results: A total of 13/15 patients have completed the trial. Utilizing Response Evaluation Criteria in Solid Tumors, 4 patients developed progressive disease, 1 patient died of disease, 5 continue to be disease-free, 1 has a complete response, and 1 has a partial response with regression of metastases lasting >16 months. Relapse-free intervals range from 18 months to 3 months. Twelve of these 13 patients (the first patient was not evaluated) developed autoimmune antibodies (anti-cardiolipin, anti-thyroglobulin or both) post-trial. Vitiligo developed in 4/13 patients, correlating with 2 patients who developed clinical tumor regression.

Conclusions: The combined immunotherapy of advanced melanoma patients with PEG-Intron® and the HAM vaccine shows evidence of synergistic immune activation that translates into clinical efficacy as seen with tumor regression combined with development of autoimmune antibodies and vitiligo.

17 SALVAGE THERAPY WITH TIMP-3 PROMOTES FAVORABLE CYTOKINE PROFILE IN RAT LIVERS AFTER SUBLETHAL TOTAL HEPATIC ISCHEMIA

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Background: Ischemia/reperfusion (I/R) injury produces an inflammatory cascade that includes tumor necrosis factor-alpha (TNF-α) converting enzyme (TACE). Pretreatment with tissue inhibitor of metalloproteinase-3 (TIMP-3) appears to convey a protective benefit to livers undergoing I/R injury.

Objectives: To determine if TIMP-3 administered 1 hour after ischemia would be a clinically relevant treatment option for livers that had undergone I/R injury.

Methods: Male Wistar rats (n=4/group) underwent our standard total warm ischemia model for 30 minutes. One hour after ischemia, all animals were injected through the vena cava with TIMP-3, a TACE-specific inhibitor, at a dosage of either 0 (saline control group) or 1,000 ng/Kg body weight (treatment group). After 6, 24, or 48 hours or 7 days of reperfusion, blood and liver tissue samples were collected after animals were euthanized. Serum TNF-α, interleukin (IL)-6, and IL-19 levels were measured by enzyme-linked immunoabsorbent assay.

Results: All animals survived sublethal hepatic ischemia. Control animals subjected to I/R injury had high levels of serum TNF-α up to 7 days after injury (59 pg/mL to 16.7 pg/mL). With TIMP-3 treatment, there was 31%–34% inhibition for the first 48 hours after injury (40.7 pg/mL to 11.3 pg/mL, $P<0.01$). On day 7, although the treated animals recovered with increased TNF-α levels, TNF-α was still 43% below that of the control animals. Cytokine IL-6 had a similar pattern to the serum TNF-α levels, with marked inhibition for the first 48 hours in TIMP-3-treated animals ($P<0.05$) that returned to baseline at 7 days. Treatment with TIMP-3 resulted in very significant inhibition (65%) of IL-19 activity at 6 hours ($P<0.001$) and 50% inhibition at 24 hours. IL-19 levels of both the control and treated animals were similar at 48 hours.

Conclusions: Salvage therapy with TIMP-3 resulted in significantly lower circulating levels of TNF-α, IL-6, and IL-19, indicating the treatment's protective effect on ischemic livers. The cytokine profile suggests that TIMP-3 administered after I/R injury may play a clinically relevant role assisting the recovery of livers that had undergone total hepatic ischemia.

18 POSTOPERATIVE TREATMENT WITH TIMP-3 PRESERVES LIVER HISTOLOGY BY PREVENTING APOPTOSIS DURING SUBLETHAL TOTAL HEPATIC ISCHEMIC INJURY IN RATS

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Background: Tumor necrosis factor-alpha (TNF-α) converting enzyme (TACE) plays a critical role in the inflammatory cascade after ischemia/reperfusion (I/R) injury. Research has proven the effective inhibition of TACE by tissue inhibitor of metalloproteinase-3 (TIMP-3) and the treatment's protective role on liver biochemistry, yet limited data demonstrate actual liver tissue preservation.

Objectives: We previously reported that TIMP-3 injected prior to I/R injury inhibits hepatic TACE expression. In this report, we administered TIMP-3 in a clinically more relevant role as a bolus injection 1 hour after the ischemic injury to examine the drug's effect on apoptosis.

Methods: Male Wistar rats (n=4/group) underwent our standard total warm ischemia model for 30 minutes. One hour after ischemia, all animals were injected through the vena cava with TIMP-3 at a dosage of either 0 (saline control group) or 1,000 ng/kg body weight (treatment group). After 6, 24, or 48 hours or 7 days of reperfusion, blood and liver tissue samples were collected after animals were euthanized. Quantitative alanine aminotransferase (ALT) levels were measured by spectrophotometer. Caspases-3/7 activity was measured from the liver tissue samples by Caspase-Glo Assay. Liver histology was undertaken by a blinded pathologist.

Results: At 6 hours, liver histology demonstrated features of early ischemic changes in both the control and treatment groups. After 7 days, the control animals showed panlobular ischemic changes with disorganized lobules and loss of clear cell borders. The treated group showed nearly normal liver parenchyma with maintained lobular architecture and intact cell borders. Control and 192.18 pg/mL). The TIMP-3-treated animals had significantly lower ALT levels for the first 24 hours (198.65 pg/mL and 118.08 pg/mL, $P<0.05$). In both control and treated animals, ALT levels returned to normal at 48 hours. The Caspases-3/7 enzyme activity in treated animals demonstrated significant inhibition for the first 24 hours.

Conclusions: Postoperative treatment with TIMP-3 preserves liver histology and biochemistry during sublethal total hepatic ischemic injury in rats. The mechanism appears to be related to the decrease of apoptosis as measured by Caspases-3/7 enzyme activity. This study suggests that TIMP-3 administered after I/R injury may have a potential clinical application in rescuing livers that have undergone injury.

19 END-TO-SIDE NEURORRHAPHY: EFFECT ON AXONAL REGENERATION AFTER DELAYED REPAIR AND ON DONOR NERVE

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Objectives: To use end-to-side repair to "babysit" the distal nerve stump to prevent chronic Schwann cell (SC) denervation and thereby promote motor axonal regeneration.

Methods: The common peroneal (CP) branch of rat sciatic nerve was cut and either subjected to 12 weeks of chronic denervation (control group) or "babysat" by cross-suturing it end-to-side into the tibial (TIB) nerve (experimental group). After 12 weeks, the proximal stump of a freshly cut TIB nerve was cross-sutured into either the babysat or chronically denervated CP nerve. After 6 weeks, we used retrograde labeling technique (fluorogold, rubyred, or both) to label and identify the numbers of TIB motoneurons that regenerated their axons into: 1) chronically denervated distal CP nerve, 2) babysat distal CP nerve, 3) sprouted into the distal CP nerve via the end-to-side repair, 4) remained in the TIB nerve stump despite end-to-side suture, or 5) sprouted into the CP nerve but also remained in the TIB nerve (double-labeled nonfunctional TIB motoneurons). The histological profiles of regenerated axons were also analyzed.

Results: A total of 373 ± 62 (mean $\pm$ SE) TIB motoneurons regenerated their axons in the control group as compared to 526 ± 69 that regenerated in the experimental group. Out of a total of 566 ± 100 TIB motoneurons, 231 ± 83 regenerated into the babysat CP distal nerve stump, 281 ± 114 remained in the TIB nerve trunk, and 55 ± 28 had axons in both the TIB and CP nerves.

Conclusions: Temporary innervations of the distal nerve stumps prevented the deleterious effect of chronic denervation on motor axonal regeneration.

20 VASCULAR RESPONSES TO GLYCERYL TRINITRATE ARE MEDIATED BY ALDEHYDE DEHYDROGENASE BUT NOT BY XANTHINE OXIDOREDUCTASE IN THE RAT

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Background: Glyceryl trinitrate (nitroglycerin, GTN) has been shown to have wide use in medicine. However, the mechanism by which GTN is converted to vasoactive nitric oxide (NO) or to S-nitrosothiol remains uncertain. It has been hypothesized that GTN is bioactivated by aldehyde dehydrogenase and possibly by other pathways to nitrite and subsequently reduced to NO. However, these mechanisms have not been clearly identified in the intact rat with several studies report conflicting results.

Methods: In the present study, the effects of the aldehyde dehydrogenase inhibitor, cyanamide, and the xanthine oxidoreductase inhibitor, allopurinol, on vasodepressor responses to GTN were investigated in the pulmonary and systemic vascular beds of the rat.

Results: The decreases in pulmonary and systemic arterial pressure in response to intravenous (IV) injections of GTN were inhibited in a selective manner following administration of cyanamide in a dose of 25 mg/kg IV, whereas a second 25 mg/kg IV dose had no additional inhibitory effect. The decreases in pulmonary and systemic arterial pressure in response to GTN were not attenuated by allopurinol, and a second 25 mg/kg IV dose had no additional inhibitory effect. In L-NAME-treated animals, cyanamide attenuated pulmonary and systemic arterial responses to GTN, and subsequent administration of allopurinol had no additional effect. When the order of administration of the inhibitors was reversed, responses to GTN were not attenuated in L-NAME-treated animals by administration of allopurinol, whereas subsequent administration of cyanamide had an inhibitory effect.

Conclusions: The results of these studies indicate that GTN can be reduced to vasoactive NO or to S-nitrosothiol in the pulmonary and systemic vascular beds of the rat by aldehyde dehydrogenase but not xanthine oxidoreductase.

21 PULMONARY AND SYSTEMIC VASODILATOR RESPONSES TO THE SOLUBLE GUANYLYL CYCLASE STIMULATOR, BAY 41-8543, ARE MODULATED BY NITRIC OXIDE

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Background: Bay 41-8543 is a nitric oxide (NO)-independent stimulator of soluble guanylyl cyclase (sGC).

Methods: In the present study, responses to intravenous (IV) injections of BAY 41-8543 were investigated under baseline and elevated tone conditions and when NO synthase (NOS) was inhibited with L-NAME.

Results: Under baseline conditions, IV injections of BAY 41-8543 caused small decreases in pulmonary arterial pressure, larger decreases in systemic arterial pressure, and increases in cardiac output. When pulmonary arterial pressure was increased to approximately 30 mmHg with an IV infusion of the thromboxane receptor agonist U46619, IV injections of BAY 41-8543 produced larger dose-dependent decreases in pulmonary arterial pressure, and the relative decreases in pulmonary and systemic arterial pressure in response to the sGC stimulator were similar. Treatment with L-NAME markedly decreased responses to BAY 41-8543 when pulmonary arterial pressure was increased to similar values (~30 mmHg) in U46619-infused and in U46619-infused plus L-NAME-treated animals. The IV injection of a small dose of sodium nitroprusside (SNP), when combined with BAY 41-8543, enhanced pulmonary and systemic vasodilator responses to the sGC stimulator in L-NAME-treated animals. The present results indicate that BAY 41-8543 has similar vasodilator action in the systemic and pulmonary vascular beds when pulmonary vasoconstrictor tone is increased with U46619.

Conclusions: These results demonstrate that pulmonary and systemic vasodilator responses to BAY 41-8543 are significantly attenuated when NOS is inhibited by L-NAME and show that vasodilator responses to BAY 41-8543 are enhanced when combined with a small dose of SNP in L-NAME-treated animals. The present results are consistent with the concept that pulmonary and systemic vasodilator responses to the sGC stimulator are NO-independent; however, the vasodilator action of the compound is greatly diminished when endogenous NO production is inhibited with L-NAME. These data show that BAY 41-8543 has similar vasodilator action in the pulmonary and systemic vascular beds in the rat.

22 VASCULAR RESPONSES TO NITRITE ARE MEDIATED BY XANTHINE OXIDOREDUCTASE AND ALDEHYDE DEHYDROGENASE IN THE RAT

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Background: Sodium nitrite has been shown to have vasodilator activity in experimental animals and in human subjects. However, the mechanism by which nitrite anion is converted to vasoactive nitric oxide (NO) is uncertain. It has been hypothesized that deoxyhemoglobin, xanthine oxidoreductase, and other heme proteins can reduce nitrite to NO. However, studies in the literature have not identified the mechanism in the intact rat, and several studies report no effect of inhibitors of xanthine oxidoreductase.

Methods: In the present study, the effects of the xanthine oxidoreductase inhibitor, allopurinol, and the aldehyde dehydrogenase inhibitor, cyanamide, on vasodepressor responses to sodium nitrite were investigated in the systemic vascular bed of the rat.

Results: The decreases in systemic arterial pressure in response to intravenous (IV) injections of sodium nitrite were inhibited in a selective manner following administration of allopurinol in a dose of 25 mg/kg IV. A second 25 mg/kg IV dose had no additional inhibitory effect. The decreases in systemic arterial pressure in response to sodium nitrite were attenuated by cyanamide and a second 25 mg/kg IV dose had no additional inhibitory effect. In L-NAME-treated animals, allopurinol attenuated responses to sodium nitrite and subsequent administration of cyanamide had no additional effect. When the order of administration of the inhibitors was reversed, responses to sodium nitrite were attenuated in L-NAME-treated animals by administration of cyanamide and subsequent administration of allopurinol had no additional inhibitory effect.

Conclusions: The results of these studies indicate that nitrite can be reduced to vasoactive NO in the systemic vascular bed of the rat by xanthine oxidoreductase and aldehyde dehydrogenase and that the mechanisms of nitrite reduction act in a parallel manner.

23 ANALYSIS OF RESPONSES TO THE RHO-KINASE INHIBITOR Y-27632 IN THE PULMONARY VASCULAR BED OF THE RAT

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Methods: The effects of the Rho-kinase inhibitor Y-27632 on the pulmonary vascular bed and on the response to hypoxia were investigated in the anesthetized rat.

Results: Under baseline conditions, intravenous (IV) injections of Y-27632 decreased pulmonary and systemic arterial pressures and increased cardiac output. The decreases in pulmonary arterial pressure were small under baseline conditions and were enhanced when baseline tone was increased with U46619. Under elevated tone conditions, decreases in pulmonary and systemic arterial pressure in response to Y-27632 were similar. Injections of Y-27632 prevented and reversed the increase in pulmonary arterial pressure in response to ventilation with a 10% O_2 gas mixture, and the response to ventilatory hypoxia was not well maintained during the period of hypoxia in the rat. The administration of L-NAME increased pulmonary arterial pressure; in L-NAME-treated animals, the response to hypoxia was increased and well maintained. Y-27632 decreased pulmonary arterial pressure and reversed the response to hypoxia in L-NAME-treated animals.

Conclusions: These data suggest that Rho-kinase is involved in the maintenance of baseline tone in the pulmonary and systemic vascular beds and is involved in the mediation of pulmonary vasoconstrictor responses to hypoxia, U46619, and L-NAME. These data also indicate that the response to hypoxia is modulated by the release of nitric oxide from the endothelium, which mediates the decline in pressure during the period of hypoxia. It is concluded that Rho-kinase and nitric oxide synthase play a major role in regulating baseline tone and the response to hypoxia in the pulmonary vascular bed of the rat.

24 MITOCHONDRIAL ALDEHYDE DEHYDROGENASE MEDIATES VASODILATOR RESPONSES OF GLYCERYL TRINITRATE AND SODIUM NITRITE IN THE PULMONARY VASCULAR BED OF THE RAT

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Background: It has been reported that mitochondrial aldehyde dehydrogenase ($ALDH_2$) catalyzes the formation of glyceryl dinitrate and inorganic nitrite from glyceryl trinitrate (GTN), leading to an increase in cGMP and vasodilation in the coronary and systemic vascular beds. However, the role of nitric oxide (NO) formed from nitrite in mediating the response to GTN in the pulmonary vascular bed is uncertain.

Objectives: To determine if nitrite plays a role in mediating vasodilator responses to GTN.

Results: In this study, intravenous injections of GTN and sodium nitrite decreased pulmonary and systemic arterial pressures and increased cardiac output. The decreases in pulmonary arterial pressure under baseline and elevated tone conditions and decreases in systemic arterial pressure in response to GTN and sodium nitrite were attenuated by cyanamide, an $ALDH_2$ inhibitor, whereas responses to sodium nitroprusside (SNP) were not altered. The decreases in pulmonary and systemic arterial pressure in response to GTN and SNP were not altered by allopurinol, an inhibitor of xanthine oxidoreductase, whereas responses to sodium nitrite were attenuated. GTN was approximately 1,000 times more potent than sodium nitrite in decreasing pulmonary and systemic arterial pressures.

Conclusions: These results suggest that $ALDH_2$ plays an important role in the bioactivation of GTN and nitrite in the pulmonary and systemic vascular beds and that the reduction of nitrite to vasoactive NO does not play an important role in mediating vasodilator responses to GTN in the intact chest rat.

25 ETEST® SYNERGY TESTING OF MEROPENEM PLUS LEVOFLOXACIN AGAINST *STENOTROPHOMONAS MALTOPHILIA*

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Background: Meropenem (MER) + levofloxacin (LEV) is a commonly used combination in adult intensive care units. *S. maltophilia* is an emerging multi-drug-resistant nosocomial pathogen.

Objectives: To evaluate LEV in combination with MER for possible synergy against *S. maltophilia*, because we could find only one similar study using only the checkerboard method.

Methods: Twenty genetically unique (rep-PCR) clinical *S. maltophilia* isolates were collected from 5/2007–6/2009 for testing using Etest MICs and synergy method with a concentration equal to the minimum inhibitory concentration (MIC) for each drug. Etest synergy was defined by a ΣFIC ≤0.5; indifference, >0.5–4. The Etest method was compared to standard time-kill assay (TKA), using 1 × MIC for both drugs and performing colony counts at 0 hours and 24 hours (synergy: ≥2 $\log_{10}$ decrease in colony-forming unit per milliliter after 24 hours by the combination compared to the most active single agent).

Results: MICs (μg/mL) were: MER, all >32; LEV, 17 isolates: 0.38–2, the remaining 3 isolates: 4, 8, and 24. Clinical and Laboratory Standards Institute interpretive standards are LEV ≤2 S; breakpoints not available for MER. Synergy with LEV + MER was seen in 12/20 (60%) of *S. maltophilia* isolates by the Etest method (ΣFICs: 0.1–0.5), with 8/20 (40%) showing indifference (ΣFICs: 0.7–1.2). TKA showed synergy in 9/20 (45%) ($\log_{10}$ change: −2.0 to −4.4) with 11/20 (55%) indifference ($\log_{10}$ change: −1.6 to +1.6).

Conclusions: Further evaluation with additional *S. maltophilia* isolates is needed to substantiate the encouraging 60% Etest synergy with MER + LEV. Regardless, *in vitro* findings may or may not translate into *in vivo* effectiveness.

26 POLYUNSATURATED FATTY ACIDS IN HUMAN AQUEOUS HUMOR

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Objectives: To determine whether lipids derived from omega-6 and omega-3 polyunsaturated fatty acids (PUFAs) are present in human aqueous humor (AH).

Methods: A total of 18 samples of AH were obtained at the time of anterior segment intraocular surgery and analyzed in masked fashion for the presence of lipids derived from PUFAs using liquid chromatography ultraviolet tandem mass spectrometry.

Results: Four of 18 samples of AH have been analyzed and demonstrated the presence of linoleic acid, an omega-6 fatty acid, and alpha-linolenic acid, an omega-3 fatty acid, with metabolites docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA). No intraoperative or postoperative complications were related to sample collection.

Conclusions: We have identified, for the first time, the presence of omega-6 and omega-3 PUFAs in human aqueous humor. The omega-3 PUFAs DHA and EPA are precursors for a novel class of mediators termed resolvins and protectins that possess pro-anti-inflammatory, pro-resolving, and neuroprotective properties. Identification of this unique class of endogenous lipid mediators in human AH can lead the way in the development of novel therapeutic agents and diagnostic tests.

27 IMPACT OF RELATIVE WALL THICKNESS ON LEFT VENTRICULAR GEOMETRY AND MORTALITY IN 47,865 PATIENTS WITH PRESERVED SYSTOLIC FUNCTION: DOES THE METHOD MATTER?

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Background: Relative wall thickness (RWT) is typically determined using 2 × posterior wall thickness (PWT)/left ventricular end-diastolic diameter (LVEDd); other methods include septal wall thickness (2 × SWT/LVEDd) or a combination of both (PWT + SWT/LVEDd). However, data showing the comparison between RWT methods are scant.

Methods: We evaluated 47,865 patients (mean age: 61.6 ± 15.4 years; 54% female) to compare three methods of RWT and to examine their impact on left ventricular (LV) geometry and mortality during an average follow-up of 1.7 years.

Results: Measurement of RWT by PWT or SWT was poorly correlated ($r=0.77$, $p<0.0001$), but both were highly correlated to RWT by PWT plus SWT ($r=0.92$–0.95, $p<0.0001$). Identification of LV geometry using different methods of RWT showed significant differences in prevalence of LV geometry. Prevalence of mortality in concentric remodeling (increased RWT but no LVH) defined by RWT using PWT was significantly higher than SWT method but lower than PWT plus SWT method. Mortality prevalence in other LV geometric patterns was not different by RWT methods. RWT determined by PWT was the strongest predictor of mortality compared to other methods, in which RWTs also were independent predictors of mortality.

Conclusions: Although all methods of RWT provide reasonable clinical accuracy for assessing LV geometry and prognosis, our results indicate that the PWT measurement is preferred, unless PWT is not easily measurable or severe septal asymmetry is present (as underestimation of RWT may occur if only PWT is used).

28 LEFT ATRIAL VOLUME AND MORTALITY PREDICTION: DOES THE METHOD OF INDEXING MATTER?

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Background: Echocardiographic left atrial (LA) enlargement (LAE) is routinely measured as LA volume (LAV) indexed to body surface area (BSA) and is a significant predictor of cardiovascular outcomes. However, such indexing could underestimate the prevalence of LAE in some populations, such as the obese. In contrast, LAV indexed to height (Ht) or Ht with allometric power ($Ht^{2.0}$ or $Ht^{2.7}$) may be better for identifying LAE, given the known relation of height with lean body mass.

Methods: We evaluated 47,865 patients (age: 61.6 ± 15.4 years; 54% female) with preserved ejection fraction to compare various indexing methods for LAV and to examine their impact on mortality during an average follow-up of 1.7 ± 1 years.

Results: All LAV indexing methods were highly correlated ($r=0.95$–0.99, $P<0.0001$). Prevalence of LAE was calculated using the upper limit of mean plus two SD as a cut point for each LAV indexed to BSA, Ht, $Ht^{2.0}$ and $Ht^{2.7}$. Prevalence of LAE determined by LAV indexed to all Ht parameters increased significantly ($P<0.0001$) with increase in body mass index (BMI). In contrast, prevalence of LAE by LAV/BSA decreased significantly ($P<0.0001$) with increasing BMI. LAV indexed to $Ht^{2.7}$ was the strongest independent predictor of mortality compared to $Ht^{2.0}$, BSA, and Ht [HR: 1.025 (1.020–1.030) vs 1.017 (1.014–1.021) vs 1.011 (1.009–1.013) vs 1.010 (1.008–1.012), $P<0.0001$, respectively], although all methods predicted mortality.

Conclusions: LAV indexed to BSA may over- or underestimate the prevalence of LAE compared to other methods in patients depending upon their obesity status. However, LAV indexed to Ht or Ht with allometric powers was unaffected by the level of obesity and appears to be preferable to indexing by BSA, which will need to be assessed in other populations.

29 LEFT VENTRICULAR GEOMETRY AND MORTALITY PREDICTION BY DIFFERENT INDEXATION METHODS FOR LEFT VENTRICULAR MASS BY OBESITY STATUS IN 47,865 PATIENTS

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Background: Echo-determined left ventricular (LV) mass (LVM) is often indexed to body surface area (BSA), but this may not accurately characterize the influence of obesity on LVM and related mortality.

Methods: We evaluated 18,630 obese [body mass index (BMI) ≥30 kg/m^2; age: 59 ± 14 years] and 29,235 nonobese (BMI <30 kg/m^2; age: 63 ± 17 years) patients with preserved ejection fraction to determine the impact of LVM indexed to either BSA or height (Ht$^{2.7}$) on prevalence of abnormal LV geometry as per standard methods [concentric remodeling (CR), and eccentric (EH) or concentric (CH) LV hypertrophy (LVH)] and mortality during a mean follow-up of 1.7 ± 1 years.

Results: Compared to the nonobese, obese patients had higher LVM index (LVM/BSA: 84 ± 30 g/m^2 vs. 88 ± 27 g/m^2, p<0.0001; LVM/ Ht$^{2.7}$: 37 ± 13 g/m^2 vs. 45 ± 15 g/m$^{2.7}$, p<0.0001). Both indices were significantly correlated, albeit less so in obese than nonobese patients (r=0.92 vs. 0.97, respectively). LVM indexed to either BSA or Ht$^{2.7}$ independently predicted mortality in both obese and nonobese groups (all p<0.0001). The LVM/BSA method produced a higher prevalence of normal and CR but lower prevalence of EH and CH compared to the LVM/Ht$^{2.7}$ method, especially in moderate (BMI 35–40 kg/m^2) and severe (BMI >40 kg/m^2) obesity. However, the LVM/BSA method had higher mortality in CR, EH, and CH compared to the LVM/Ht$^{2.7}$ method, especially in obesity.

Conclusions: Subtle differences in the classification of LV geometry between the two LVM indexing methods were noted, particularly in patients with more marked degrees of obesity. LV geometric classifications using LVM corrected by either BSA or Ht$^{2.7}$ predict mortality, both in obese and nonobese patients.

30 ECHOCARDIOGRAPHIC DETECTION OF LEFT VENTRICULAR HYPERTROPHY: WHICH INDEXING METHOD IS THE BEST PREDICTOR OF CLINICAL OUTCOMES?

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Background: Left ventricular hypertrophy (LVH) is a powerful independent risk factor predicting subsequent cardiovascular morbidity and mortality and is best determined echocardiographically as left ventricular mass (LVM) indexed to body size [either body surface area (BSA) or height$^{2.7}$ (Ht$^{2.7}$)]. However, considerable controversy exists regarding which of these two methods is superior for the determination of LVH and its subsequent outcomes.

Methods: We evaluated 47,865 patients with preserved ejection fraction to determine the impact of LVM indexed to either BSA (LVH=LVM index >104 g/m^2 in women and 116 g/m^2 in men) or Ht$^{2.7}$ (LVH=LVM index >51 g/m$^{2.7}$) on the prevalence of LVH and subsequent mortality during an average follow-up of 1.7 ± 1 years.

Results: Deceased patients (n=3,653) had significantly higher LVM (176.3 ± 69 g vs. 166.3 ± 62.3 g, p<0.0001) and prevalence of LVH [by LVM/BSA (25.7% vs. 14.7%, p<0.0001) or by LVM/Ht$^{2.7}$ (26.2% vs. 17.7%)] than survivors (n=44,212). Both LVM indices were significantly correlated (r=0.93, p<0.0001) and were concordant in determining the presence or absence of LVH in 93% of patients. In the 7% (n=3,214) of patients where categorical LVH was discordant between the two indexing methods, LVH determined by LVM indexed to BSA predicted an increase in mortality compared to patients without LVH (15.2% vs. 6.7%, p<0.0001) whereas LVH determined by LVM indexed to Ht$^{2.7}$ did not (7% vs. 6.7%, p=NS).

Conclusions: Classification of LVH by echocardiography using LVM indexed to BSA is superior to LVM indexed to Ht$^{2.7}$ in predicting subsequent mortality.

31 IMPACT OF LEFT ATRIAL VOLUME INDEX AND LEFT VENTRICULAR GEOMETRY ON MORTALITY IN OBESE VERSUS NONOBESE ELDERLY PATIENTS WITH PRESERVED EJECTION FRACTION

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Background: Left atrial volume index (LAVi) and left ventricular (LV) geometry predict cardiovascular events. Although obesity is a risk factor for cardiovascular diseases, studies have noted a paradox regarding obesity and prognosis. To our knowledge, no studies have determined the impact of LAVi and LV geometry on mortality by obesity status in elderly patients with preserved ejection fraction (EF).

Methods: We evaluated 16,901 patients aged ≥70 years with preserved EF, including 4,529 obese as well as 12,372 nonobese patients, to determine the impact of LAVi and LV geometry on mortality during an average follow-up of 1.7 ± 1 years.

Results: Obese patients had higher LAVi than nonobese patients (35.6 ± 12.4 vs 33.7 ± 10.6, p<0.0001). Abnormal LV geometry occurred more commonly in obese than nonobese patients (61% vs 52%, p<0.0001). In obese patients, concentric remodeling was the most prevalent abnormal pattern (40%), with eccentric and concentric LV hypertrophy occurring in 11% and 15% of obese patients, respectively, compared to nonobese patients (32%, 9%, and 11%, respectively). Moreover, a significant upward trend (p<0.0001) was observed in LAVi, LV mass index (LVMI), and relative wall thickness (RWT) with increasing age- and gender-adjusted quartiles of body mass index (BMI). Overall mortality was considerably lower in obese than nonobese patients (3.4% vs. 10.8%, p<0.0001). Although, age- and gender-adjusted top vs. bottom quartiles of LAVi, LVMI, and RWT showed significant higher mortality (p<0.0001) in both obese and nonobese patients, the difference was far greater in obese patients. In both groups, higher age, RWT, and LAVi were independent predictors of mortality. Of note, increasing BMI was associated with lower mortality [OR: 0.94 (0.93–0.96), p<0.0001] in nonobese compared to obese patients where mortality increased with BMI [OR: 1.05 (1.03–1.07), p<0.0001]. Other mortality predictors were male gender and low EF (nonobese).

Conclusions: Although an obesity paradox exists, in that obesity is associated with higher prevalence of structural abnormalities but lower mortality than in nonobese patients, LAVi and LV geometric abnormalities are more prevalent in obese than nonobese elderly patients with preserved EF and are associated with increases in mortality.

32 IN ISCHEMIC CARDIOMYOPATHY WITH REDUCED EJECTION FRACTION, THE INTERVAL BETWEEN T-WAVE PEAK AND T-WAVE END PREDICTS BOTH APPROPRIATE ICD THERAPY AND OVERALL SURVIVAL

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Background: A longer interval between the peak of the T wave and the end of the T wave (Tp-Te) is a surrogate measure of total dispersion of ventricular repolarization and retrospectively correlates with tachyarrhythmia in various models and patient groups. Whether Tp-Te predicts spontaneous ventricular arrhythmia or death in patients with ischemic cardiomyopathy with a reduced ejection fraction is unknown.

Methods: We prospectively evaluated 332 patients (75% male, age 67 ± 11 years) with coronary artery disease, left ventricular injection fraction ≤35% (mean, 25% ± 9%), and an implanted cardioverter-defibrillator (ICD). At baseline, the average Tp-Te in electrocardiogram leads V3–V6 was measured using a GE Healthcare computer algorithm. Follow-up for appropriate ICD therapy and death was conducted via chart review, device interrogation, and Social Security Death Index (SSDI) query.

Results: Mean Tp-Te was 100 ± 20 ms (IQR, 86–112 ms). Over 17 ± 12 months of device follow-up, 61 (18%) patients had appropriate ICD therapy; over 25 ± 12 months of SSDI follow-up, 63 (19%) patients died. Longer Tp-Te predicted both appropriate ICD therapy (RR per 10 ms increase in Tp-Te: 1.14 [1.01–1.29], p=0.035) and mortality (RR per 10 ms, 1.19 [1.05–1.34], p=0.005). Two-year event rates for ICD therapy: Q1, 6%; Q2, 26%; Q3, 41%; and Q4, 32%; and for death: Q1, 9%; Q2, 16%; Q3, 16%; and Q4, 26%.

Conclusions: In patients with ischemic cardiomyopathy with a depressed ejection fraction, longer Tp-Te is strongly predictive of both appropriate ICD therapy and overall mortality.

33 INCREASED FREQUENCY OF CIRCULATING CXCR5$^+$CD57$^+$CD4$^+$ FOLLICULAR T HELPER CELLS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Production of high-affinity autoantibodies is central to the pathogenesis of systemic lupus erythematosus (SLE). CXCR5$^+$CD57$^+$CD4$^+$ follicular T helper cells (T_{FH}) play an important role in the generation of high-affinity autoantibody secreting, long-lived plasma cells in part through their production of IL-21.

Objectives: To compare the frequency of CXCR5+CD57+CD4+ follicular T helper cells in the peripheral blood of SLE patients with healthy controls along with their expression of interleukin (IL)-21.

Methods: Peripheral blood was collected from five patients with SLE as defined by American College of Rheumatology criteria and five healthy controls. The distribution of T cell subsets was defined by the expression of surface markers (CD3, CD4, CD8, CD57, CXCR5) determined through flow cytometry. IL-21 expression on the T cell subsets was determined by intracellular staining and detected by four-color flow cytometry.

Results: Our study demonstrated a significantly increased population of CXCR5$^+$CD57$^+$CD4$^+$ T cells in the peripheral blood of SLE patients compared to healthy controls ($P<0.01$). These CXCR5$^+$CD57$^+$CD4$^+$ T cells also expressed the costimulatory molecule ICOS. Intracellular staining showed that the CXCR5$^+$ CD57$^+$ cells expressed significant higher IL-21 than CXCR5$^-$CD57$^-$CD4$^+$ T cells and CD8$^+$ T cells.

Conclusions: This is the first study that demonstrates circulating CXCR5$^+$CD57$^+$CD4$^+$ T cells in SLE patients. This could reflect an excessive T_{FH} response in SLE that would suggest increased circulating IL-21 secreting T_{FH} are central to the B cell hyper-reactivity underlying the pathogenesis of SLE.

34 THE INFLUENCE OF IMMUNOSUPPRESSIVE THERAPY ON INFECTION RISK IN RHEUMATOID ARTHRITIS

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Background: Patients with rheumatoid arthritis (RA) are at increased risk for infection as a result of their underlying disease. Furthermore, the vast majority of these patients require immunosuppressive therapy to control their disease activity. Current guidelines recommend discontinuing immunosuppressive therapy while RA patients are being treated for infection, due to concerns that these drugs exacerbate their underlying immunocompromised state.

Objectives: To develop an evidence-based strategy for managing immunosuppressive therapy in RA patients with an infection.

Methods: We reviewed numerous retrospective large cohort studies examining the influence of immunosuppressive therapy on RA infection risk.

Results: There was a dose-related increased risk of pneumonia associated with the use of prednisone beginning with doses as low as 5 mg. The use of hydroxychloroquine or sulfasalazine was associated with a significantly decreased incidence of infection. The use of methotrexate or leflunomide appeared to be fairly neutral with regards to infection risk. The use of tumor necrosis factor-alpha (TNF-α) inhibitors increased the risk of pneumonia by as much as four-fold, but this risk appears to decline after 6 months, with a neutral risk at 2 years.

Conclusions: While it appears reasonable to hold TNF-α antagonist therapy and prednisone while RA patients are infected, the data do not support the current common practice of holding disease-modifying antirheumatic drug (DMARD) therapy during an infection. Prospective outcome studies are needed to determine whether continuing DMARD therapy during treatment for mild to moderate infections might be safe or perhaps even beneficial.

35 THE INFLUENCE OF IMMUNOSUPPRESSIVE THERAPY ON INFLUENZA, PNEUMOCOCCAL, AND HEPATITIS B VACCINE IMMUNOGENICITY IN RHEUMATOID ARTHRITIS

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Background: The pneumococcal, influenza, and hepatitis B vaccines are proven, simple, and effective means for preventing morbidity and mortality in the general population. Although patients with rheumatoid arthritis (RA) suffer increased morbidity and mortality from these diseases, their vaccination rates ironically tend to be lower than in the general population. The reasons for this are perhaps due to misconceptions regarding vaccine efficacy in patients with RA, including the perceived effect of concomitant immunosuppressive therapy.

Methods: We reviewed numerous controlled studies examining immunogenicity of the influenza, pneumococcal, and hepatitis B vaccines in RA patients along with the influence of immunosuppressive therapy.

Results: The use of tumor necrosis factor-alpha inhibitors appears to mildly decrease influenza vaccine immunogenicity in RA patients. The use of methotrexate appears to mildly decrease pneumococcal vaccine immunogenicity in RA patients. Although rituximab appears to decrease influenza vaccine immunogenicity in RA patients vaccinated 1–2 months postinfusion, this immunogenic response is modestly restored when vaccinated at 6–10 months postinfusion. Rituximab also appears to significantly blunt the immunogenic response to the pneumococcal vaccine. The hepatitis B vaccine series was immunogenic in 68% of RA patients at 1 month after completion of the series in a small study.

Conclusions: While certain immunosuppressive therapies appear to negatively influence vaccine immunogenicity in RA patients, these patients should nonetheless be vaccinated appropriately. The effect of timing vaccine administration around the use of immunosuppressive therapy needs to be studied furthered in RA patients, so we can optimize their vaccine immunogenic response.

36 ADDRESSING THE NEED FOR ZOSTER VACCINATION IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) patients are at increased risk for herpes zoster infection as a result of their underlying disease. The therapeutic use of TNF-alpha (TNF-α) monoclonal antibodies has been found to not only further increase this risk but also to increase the frequency of severe zoster infections. While the zoster vaccine has proven successful in preventing herpes zoster infection and reducing post-herpetic neuralgia in healthy individuals ≥60 years, safety concerns have limited the use of this live vaccine in patients with RA.

Objectives: To develop an evidence-based strategy for vaccinating RA patients with the zoster vaccine.

Methods: We reviewed the known safety data regarding the use of the live zoster vaccine in immunocompromised patients.

Results: Although no zoster vaccine safety data for RA patients currently exist, the smaller dose of varicella vaccine has been shown to be well tolerated in several populations of immunocompromised children, including those with leukemia and advanced HIV infection and organ transplant recipients.

Conclusions: Current recommendations advise against vaccinating RA patients who are receiving TNF-α inhibition for fear of possible adverse reaction, but these recommendations are not based on scientific evidence. Pilot studies are needed to determine whether live zoster vaccination is safe to use in RA patients receiving TNF-α inhibitors, as these patients should benefit the most from this preventative strategy. Furthermore, current recommendations should be extended to include RA patients of all ages for zoster vaccination unless otherwise contraindicated.

37 PATTERNS OF CARDIOVASCULAR RISK AND DISEASE AMONG PEOPLE WITH TYPE 2 DIABETES STARTING INSULIN: BASELINE CHARACTERISTICS IN THE CREDIT STUDY

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38 PATIENT-DIRECTED TITRATION FOR ACHIEVING GLYCEMIC GOALS USING A ONCE-DAILY BASAL INSULIN ANALOGUE: AN ASSESSMENT OF TWO DIFFERENT FASTING PLASMA GLUCOSE TARGETS—THE TITRATE™ STUDY

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39 PREDICTIVE VALUE OF THE EL-GANZOURI MULTIVARIATE RISK INDEX FOR DIFFICULT TRACHEAL INTUBATION USING THE CONVENTIONAL MILLER LARYNGOSCOPE BLADE AND THE GLIDESCOPE VIDEO LARYNGOSCOPE AS AN AIRWAY RESCUE DEVICE

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Background: Failure to intubate and adequately ventilate patients remains a leading cause of perioperative morbidity and mortality. Accurate preoperative prediction of potential difficulty with orotracheal intubation can reduce the incidence of complications by alerting anesthesia providers to adequately prepare for and take additional precautions to secure the patient's airway. The El-Ganzouri multivariate risk index consists of seven independent preoperative physical characteristics that have been shown to demonstrate varying degrees of sensitivity or specificity to preoperatively predict difficult orotracheal intubation. However, these studies have not been researched using the Miller (straight) laryngoscope blade.

Results: In an interim analysis of 600 adult patients, we failed to identify any single risk factor for predicting difficult intubation using the El-Ganzouri multivariate risk index. Although the intubation wand, rather than the GlideScope or the Macintosh blade, is the preferred rescue airway device following the initial attempt at orotracheal intubation with the Miller laryngoscope blade, our study suggested that rescue videolaryngoscopy provides a higher degree of successful attempts at orotracheal intubation.

Conclusions: These data suggest that the intubation wand may be a less preferred airway rescue device in difficult orotracheal intubation when compared to videolaryngoscopy.

40 SIX-MINUTE WALK DISTANCE AT SIX MONTHS POST-LUNG TRANSPLANT IS NOT PREDICTIVE OF MORTALITY

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41 SIX-MINUTE WALK DISTANCE AT SIX MONTHS POST-LUNG TRANSPLANT FOLLOWS A GAUSSIAN DISTRIBUTION

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42 SELECTIVE MANAGEMENT OF THE URETHRA AT TIME OF PROLAPSE REPAIR: AN ASSESSMENT OF POSTOPERATIVE INCONTINENCE AND PATIENT SATISFACTION

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Background: In women presenting with symptomatic pelvic organ prolapse (POP) in the absence of signs or symptoms of stress urinary incontinence (SUI), the literature supports the selective use of an anti-incontinence procedure. It has been our experience that the vast majority of women without symptomatic or occult SUI will not leak with prolapse surgery alone and no concomitant anti-incontinence procedure. We report our outcomes with patients who underwent selective management of the urethra at the time of POP repair. Our primary endpoints are patient satisfaction and self-reported continence.

Methods: Patients who underwent surgery for advanced POP were selected from our database. All charts were reviewed to determine whether a concomitant anti-incontinence procedure was performed. Patients were excluded if postoperative follow-up was less than 1 year. Patients were contacted via telephone to obtain responses to three validated questionnaires: the Urogenital Distress Inventory (UDI-6), Patient Global Impression of Improvement (PGI-I), and Medical, Epidemiological, and Social Aspects of Aging (MESA).

Results: A total of 42 patients met inclusion criteria; 30 completed responses to all questionnaires. Patients were separated into two groups: those who underwent prolapse repair alone (n=14) and those who underwent both prolapse repair and suburethral sling (n=16). The mean UDI-6 scores were 3.71 in the prolapse-only group and 2.31 in the concomitant sling group (p=0.219). The MESA urge component was 1.29 in the prolapse-only group and 2.69 in the concomitant sling group (p=0.244), and the MESA stress component was 3.14 in the prolapse-only group and 3.00 in the concomitant sling group (p= 0.918). The PGI-I did not reveal a statistical difference between the two groups. One patient with a prolapse-only repair returned with incontinence and underwent a secondary sling procedure. Patients who underwent a concomitant sling had a higher urge component and a lower stress component compared to the patients that underwent prolapse-only repair; however, these differences were not statistically significant.

Conclusions: Patients with advanced POP who do not have a concomitant suburethral sling at the time of their prolapse repair have continence and satisfaction outcomes that are equivalent to those who do undergo concomitant suburethral sling and prolapse repair. The decision to perform a concomitant prophylactic anti-incontinence procedure at the time of advanced prolapse repair should be tailored to the individual patient.

43 ROBOTIC URETERAL REIMPLANTATION FOR IATROGENIC INJURIES AND BENIGN DISEASE

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Background: Ureteral reimplantation is the most definitive treatment of distal ureteral pathology associated with gynecologic disease and surgery. Robotic ureteral reimplantation offers a less invasive approach to procedures.

Objectives: To evaluate the safety, efficacy, and morbidity of robotic ureteral reimplantation used to treated distal ureteral pathology associated with gynecologic disease and surgery.

Methods: A retrospective analysis was performed of all patients who underwent robotic-assisted laparoscopic ureteral reimplantation. Data recorded included patient age, gynecologic diagnosis, blood loss, operative time, type or reimplantation, complications, postoperative imaging, urinary symptoms, serum creatinine, and length of hospital stay.

Results: Five patients underwent robotic ureteral reimplantation from July 2006 to December 2008. Four patients experienced iatrogenic ureterovaginal fistula, and one patient had an endometrioma-associated ureteral stricture. Mean age of the study group was 37.2 (31–44) years. Minimal blood loss was reported. Mean hospital stay was 1.6 (1–3) days. Mean operative time was 246.6 (175–374) minutes. Types of reimplants were three nonrefluxing and two refluxing. No surgical complications were reported. Mean postoperative serum creatinine was 0.82 (0.7–1.1). Two patients refused postoperative imaging; the remaining three enjoyed resolution of either their hydronephrosis or urinary extravasation on postoperative imaging. Urinary leakage resolved in all four patients with ureterovaginal fistulas.

Conclusions: Robotic ureteral reimplantation is safe and effective for the treatment of gynecologic-associated ureteral pathology. Long-term follow-up is needed.

44 MODIFIED LATZKO PROCEDURE (PARTIAL COLPOCLEISIS) FOR VESICOVAGINAL FISTULA: TECHNIQUE AND OUTCOMES

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Background: The Modified Latzko procedure historically has been a successful approach to transvaginal treatment for vesicovaginal fistula (VVF). This procedure is reproducible and can be performed for most fistulas.

Objectives: To highlight the principles of the repair and summarize our experience.

Methods: A total of 17 patients who presented with fistulas were repaired via the Latzko technique. The key components of the procedure include: 1) adequate exposure of the apex of the vagina; 2) a circumferential, full thickness dissection of the vaginal wall to expose the fistula; 3) isolation and closure of the fistula; 4) imbricating sutures to complete the partial colpocleisis (serves as interposition); and 5) reclosure of the vaginal cuff. A retrospective chart review was completed to assess outcomes and operative experience.

Results: Ages of the 17 patients ranged from 28–80 years. No intraoperative complications occurred, including bowel, ureteral, or bladder injury. A blood loss of 600 cc was encountered in 1 patient. No complaints of sexual dysfunction were recorded. Of the 17, 88% were discharged the following day, and catheter drainage was maintained for 3–4 weeks. Sixteen (94%) had successful resolution after the primary repair, while 1 patient had failed abdominal repair. Of the 16, 1 patient had a recurrence 2 years following the primary procedure due to an inclusion cyst.

Conclusions: The Latzko procedure is a reproducible, efficacious alternative approach to the transvaginal correction of VVF. Results are excellent and complications are minimal. This procedure should be considered as the primary repair of VVF.

45 STUDY OF THE RELATIONSHIP BETWEEN UNEXPLAINED ELEVATED MATERNAL SERUM ALPHA-FETOPROTEIN AND ADVERSE PREGNANCY OUTCOME

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Objectives: To evaluate the relationship between unexplained elevated maternal serum alpha-fetoprotein (MSAFP) and adverse pregnancy outcomes. We sought to review pregnancy and fetal/neonatal complications in patients with unexplained elevated MSAFP and compare their outcomes to patients with normal MSAFP.

Methods: A retrospective chart review was performed to search for patients with an elevated MSAFP (≥2.5 MoM). Billing reports from May 2005-February 2009 with the diagnosis code for abnormal quadruple screen were reviewed. Those charts were then extracted, and the patients with unexplained elevated MSAFP were placed in the study. Variables recorded included pregnancy history, pregnancy outcome, and fetal outcome. Patient weight, age, and race were also recorded. A control group of patients with normal MSAFP values was used for comparison. Chi square and the Fisher exact test were used for statistical analyses.

Results: A total of 44 patients were entered into the study in the abnormal group and 45 in the control group. The mean age of both groups was 27 ± 6.54 years. The mean weight of the abnormal group was 173 ± 52 lbs, compared to 186 ± 61 lbs for the control group. The abnormal group delivered earlier, at 37.9 weeks' gestational age, versus 38.5 weeks in the control group. The abnormal group had lower birth weights—mean of 2,869 g—compared with 3,311 g for the control group. The incidence of adverse fetal outcome was 22.7% in the abnormal group and 11.1% in the control group, intrauterine growth retardation (IUGR) and preterm delivery (<32 weeks' gestational age) occurring most frequently. Preeclampsia was also more frequent in the abnormal group than the control (15.9% verses 8.9%).

Conclusions: Patients with unexplained elevation of MSAFP were found to have higher adverse pregnancy outcomes, such as IUGR, preterm delivery, and preeclampsia.

46 PARADIGM SHIFTS IN THE TREATMENT OF ABDOMINAL AORTIC ANEURYSM: TRENDS IN 721 PATIENTS BETWEEN 1996–2008

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Objectives: To evaluate longitudinal trends in abdominal aortic aneurysm (AAA) management after availability of later-generation endografts.

Methods: We retrospectively analyzed non-suprarenal AAA repairs between 1/1/96 and 12/31/08 performed at a single institution. Patients were stratified by treatment type [endovascular aneurysm repair (EVAR) vs. open] and the presence or absence of rupture, and 30-day mortality rates were compared with Fisher's exact test.

Results: Over a 13-year period, 721 patients underwent AAA repair, 56.9% (n=410) with EVAR and 43.1% (n=311) open. A bimodal distribution of EVAR usage was observed, with initial escalation in the 1990s to 70%. The nadir of EVAR usage occurred in the early 2000s (40%), correlating with more conservative EVAR utilization after the limitations of first-generation endografts were understood. Between 2005 and 2008, EVAR utilization increased to an average of 84%.

The overall 30-day mortality rate for the entire cohort (including ruptured AAA) was 3.8%, 2% (8/410) for EVAR and 6.1% (19/311) for open repair ($p<0.05$). Ruptured AAA had a mortality rate of 0% (n=0/8) for EVAR vs. 31% (n=9/29) for open, $p=0.16$. Non-ruptured AAA mortality was 2% (8/402) for EVAR vs. 3.6% (10/282) for open, $p=0.23$. Both EVAR and open repair had reductions in mortality in the latter half of the series, combining to provide a significant decrease in overall mortality for patients treated most recently (2003–2008, 1.8%) compared to the earlier time period (1996–2002, 4.9%), $p<0.05$). Open AAA repair became more complex during the study period; the average rate for juxta-renal open AAA repair was 17.7% (range 6.5%–34.6%) between 1996 and 2002 compared to 55.6% (range 29.6%–100%) between 2003 and 2008 ($p<0.05$).

Conclusions: AAA treatment has undergone a profound and sustained paradigm shift, now averaging 84% of repairs performed with EVAR between 2005 and 2008. Overall mortality from AAA repair, including ruptures, was reduced 64% (from 4.9% to 1.8%) over the 13-year study period. Although both EVAR and open repair had improved mortality in the latter half of the series, the primary driver in reduced mortality for AAA repair has been the shift to EVAR

47 ENDOVASCULAR DEBRANCHING OF THE AORTIC ARCH DURING THORACIC ENDOGRAFT REPAIR

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Background: Treatment of complex thoracic aortic pathology increasingly requires coverage of one or more aortic arch vessels. Endovascular debranching can reduce or eliminate the need for surgical bypass. In this study, we evaluate our initial experience with planned endovascular debranching of the aortic arch.

Methods: During a 13-month period, 9 patients were treated with endovascular debranching during thoracic endograft placement. Balloon expandable (n=7) or self-expanding stents (n=2) were deployed (innominate, n=2; left common carotid, n=2; left subclavian, n=5) along with either TAG (Gore, n=8) or Talent (Medtronic, n=1) endografts. Four patients required 5 surgical bypasses to additional arch vessels (right to left common carotid artery, n=2; left common carotid to subclavian artery, n=3).

Results: Indications for thoracic endograft placement were: aortic transection (n=4), aortic aneurysm (n=2), aortotracheal fistula (n=1), contained aortic aneurysm rupture (n=1), and acute aortic dissection (n=1). Endografts were deployed into zones 0 (n=2), 1 (n=2), and 2 (n=5). Technical success of endovascular debranching was attained in 8 patients, with maintenance of branch perfusion and absence of endoleak. Perioperative morbidity included one myocardial infarction and one death. During subsequent follow-up (range 2–9 months), there were no instances of endoleak secondary to the endo-debranching. All endo-debranched vessels maintained primary patency.

Conclusions: Endovascular debranching permits planned extension of the thoracic endograft over arch vessels while further minimizing the need for open reconstruction. Short-term results indicate technical feasibility of this approach. Long-term outcomes remain undefined.

48 DOES EARLY POUCH EVALUATION LEAD TO INCREASED POUCH COMPLICATIONS?

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49 DOES STOPPING CLOPIDOGREL FOR COLONOSCOPY CAUSE THROMBOEMBOLIC EVENTS?

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Background: The American College of Clinical Pharmacology recommends stopping clopidogrel for 7–10 days prior to any planned invasive procedure. No data relate to the thromboembolic sequelae of stopping clopidogrel.

Objectives: We hypothesized that holding clopidogrel for 7 days prior to colonoscopy would have no adverse effect with regard to bleeding or thromboembolic complications.

Methods: Over a 3-year period, patients on clopidogrel having colonoscopy were followed for bleeding and thromboembolic events. Patient demographics, reason for antiplatelet therapy, date of stopping clopidogrel, and any admits to the hospital for 60 days after colonoscopy were included in our data set.

Results: A total of 253 patients were found to be on clopidogrel prior to colonoscopy; 39 were lost to follow-up. The patients were asked to hold their clopidogrel for 7 days prior to the colonoscopy. Median days off clopidogrel were 7. Three patients were hospitalized for bleeding, and 3 patients had thromboembolic events within 60 days of colonoscopy. There was no significance to the timing of stopping clopidogrel in the patients with bleeding episodes ($p=0.5121$). Of the 3 patients who had thromboembolic events, 1 patient thrombosed an arteriovenous graft and 2 with ischemic changes on electrocardiogram. No statistical difference between last dose of clopidogrel and thromboembolic event was found ($p=0.3589$). Patients experienced no cardiac stent failures, and no patients died.

Conclusions: Stopping clopidogrel for 7 days prior to colonoscopy—except in patients with drug-eluding stents—is safe with no significant increase in long-term bleeding or thromboembolic complications.

50 DOES CATHETER DRAINAGE TIME AFFECT OUTCOME OF PERIANAL ABSCESSES?

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51 APPLICATION OF FUNCTIONAL ELECTRICAL STIMULATION DURING SURGICAL RELEASE IN SEVERE CARPAL TUNNEL SYNDROME IMPROVES REINNERVATION OF THENAR MUSCLE

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Background: Regeneration of injured nerves declines as a function of time and distance due, in part, to chronic axotomy and Schwann cell denervation prior to target reinnervation. A largely unrecognized site of delay is the surgical suture site where, in rats, 4 weeks is required for all neurons to regenerate their axons across the site. Low frequency stimulation for just 1 hour after surgery accelerates axonal regeneration across sutures.

Methods: This randomized controlled trial examined the effect of electrical stimulation on the number of reinnervated motor units in the thenar muscles after carpal tunnel release surgery in moderate to severe carpal tunnel syndrome. Within 15 minutes of surgery, the median nerve was electrically stimulated at 20 Hz for 1 hour via implanted stainless steel electrodes. Thereafter, the electrodes were removed. At 2 time points prior to surgery and at time intervals of 3 months post-surgery, motor unit number estimates (MUNE) were made using electromyographic recordings from the thenar eminence muscles in response to maximal stimulation and from single motor units.

Results: In the control group, MUNE did not increase significantly even after 12 months of release surgery. In contrast, in the experimental group, there was a trend for MUNE to increase above preoperative values by 3 months and significantly elevate by 6–8 months after surgery. The number of motor units attained normal values by 12 months, demonstrating that all of the axotomized median motoneurons had regenerated their axons to reinnervate the thenar eminence musculature. Measurements of conduction velocity of both sensory and motor nerves were consistent with the MUNE data. Behavioral tests, including the Purdue Pegboard Test, also verified the more rapid functional recovery after electrical stimulation.

Conclusions: Application of functional electrical stimulation during surgical release in severe carpal tunnel syndrome improves reinnervation of thenar muscle.

52 VITAMIN D SUPPLEMENTATION IN BREASTFED INFANTS: A PROSPECTIVE TRIAL-RECRUITMENT PROBLEM ENCOUNTERED ALONG THE WAY

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Background: Exclusive breastfeeding of newborns is more common because of the well-documented benefits to mother and baby; however, there are concerns about whether breast milk has sufficient vitamin D to prevent rickets. Anticipating this, the American Academy of Pediatrics (AAP) recommends universal vitamin D supplementation (200 IU/day) from 2 months of age, but few studies support these recommendations.

Objectives: To compare vitamin D supplementation with placebo control in breastfed children.

Methods: After obtaining approval from the Ochsner Institutional Review Board (2006-186A) normal newborns (breast milk intake >50% of total) were randomized into three study groups: no supplementation, 200 IU per day from 2 months, and 200 IU per day from birth. Blood samples and questionnaires were collected at birth and 2, 4, and 6 months of age. Our goal was to recruit 450 patients in 2 years; however, after 1 year, only 42 patients were recruited (6 patients have completed the study).

Results: We screened 757 infants from July 2007-December 2007. A total of 408 (53%) were breastfed postpartum; 94% of these mothers were approached, but only 5% agreed to participate in our study. The major reasons given for not wanting to participate were being not interested in a research study (26.5%), not willing to give a daily medication (10.3%), not breastfeeding at least 50% of the time (8.6%), and not wanting blood tests (5.9%). Retention among the recruited patients was also very low, with 66% dropping out in the first 2 months. The most common reason for dropping out of the study was cessation of breastfeeding.

The blood samples collected so far in our study were analyzed for calcium, phosphorus, parathyroid hormone, 25-hydroxyvitamin D, alkaline phosphatase, and osteocalcin (cord blood at birth). There was no apparent difference between the placebo and vitamin D-treated groups in the levels of any of these measurements at any time point; however, we do not yet have sufficient power in the study to support a negative conclusion. One case of rickets and one case of hypervitaminosis D have been reported by the pediatric endocrinologist at Ochsner; neither patient was enrolled in the study. A retrospective chart review of pediatric practices at Ochsner revealed that only 5% of breastfed infants receive vitamin D supplementation, revealing poor compliance with the AAP recommendations.

Conclusions: We recommend that the health care professionals should educate mothers of the importance of vitamin D and inform them of the current recommendations until future research can determine whether or not vitamin D supplementation is required to prevent rickets in breastfed infants.

53 IS HOME MONITORING OF SINGLE-CHAMBER IMPLANTABLE CARDIOVERTER DEFIBRILLATORS COST EFFECTIVE?

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Background: Implantable cardioverter defibrillators (ICDs) are important in the treatment of patients who are at risk of sudden cardiac death. To allow for continuous follow-up in these patients, newer ICDs have remote-monitoring capabilities (HM). This HM service enables the doctors to safely follow these patients, resulting in fewer in-clinic consultations.

Objectives: To investigate the cost-effectiveness of single-chamber ICD HM compared to standard in-clinic follow-up.

Methods: After Institutional Review Board approval, the ICD database was used to identify patients with an ICD capable of remote monitoring. Data collected included distance and time traveled to clinic. Costs incurred were calculated based on average miles/gallon, cost of gasoline, and average salary based on US Census Bureau median data. Patients were categorized into two groups: ≥2 hours' travel and <2 hours' travel. Those with ≥2 hours' travel time to clinic were also listed as missing a day's work and those <2 hours a half day's work. The cost of single-chamber ICD evaluations in clinic ($71.41) was also added. Theses two groups (<2 and ≥2 hours) were then compared to the cost of simple HM $102.

Results: We identified 32 patients with the ability to perform home monitoring. Eleven were in the <2 hours group, with an average 31 miles traveled at an estimated cost of $3.80 and half-day salary of $73.60, plus the cost of ICD evaluation in clinic, for a total cost of $179.40. There were 21 patients in the ≥2 hours group, with an average of 156 miles traveled at an estimated cost of $19.24 and full-day salary of $142.70, plus the cost of ICD evaluation in clinic, for a total cost of $233.35. Comparisons between these groups (<2 hours=$179.40, ≥2 hours=$233.35) versus the HM group ($102) revealed that HM is more cost effective than regular clinic visits for both travel groups ($p<0.01$).

Conclusions: Home monitoring of patients with a single-chamber ICD is significantly less expensive than in-clinic ICD evaluations. Home monitoring should be encouraged for all patients with capable devices.

54 A NEW FORM OF EPICARDIAL PACING UTILIZING BIPOLAR SCREW-IN LEADS

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Background: Many pediatric patients require implantation of a pacing system, consisting of a pacemaker and lead(s), to help maintain a normal heart rate and rhythm. Often these systems require epicardial implantation due to either the patient's size or intracardiac anatomy.

Objectives: To evaluate a new bipolar epicardial screw-in pacing lead reported to offer better sensing and pacing performance.

Methods: After Institutional Review Board approval, the surgical database was used to identify patients who had undergone implantation of a St. Jude Medical Enpath Myopore Bipolar epicardial lead. Data collected included indication for pacing, sensitivity, thresholds, impedance, and complications. Data points were split into four categories: day 0, <1 month, 1–3 months, and >3 months post-implant.

Results: The Enpath Myopore Bipolar lead was implanted in 8 patients. There were three atrial (A) leads and seven ventricular (Ven) leads. With regard to the A lead, its acute threshold was 1.0 Volt (V) at pulse width (pw) of 0.5 ms, the current was 2.7 mA, and impedance 541 ohms. Follow-up for the three A leads revealed no significant change in threshold, current, and impedance. The acute Ven threshold was 1.48 V at pw of 0.5 ms, current of 5.2 mA, and impendence of 780 ohms. Follow-up revealed increased V thresholds: one that decreased (1.4 V to 1.0 V) and three that increased (1.7 V to 2.5 V). There was no significant change in sensing, current, or impedance during follow-up. There are no failed leads or complications.

Conclusions: This new bipolar epicardial lead appears to be effective for pacing patients. In short-term follow-up, the lead performed satisfactorily at pacing and sensing. Further follow-up is needed to evaluate the long-term success of this lead.

55 USE OF TRANSESOPHAGEAL ELECTROPHYSIOLOGY STUDIES IN RISK ASSESSMENT OF ASYMPTOMATIC VENTRICULAR PRE-EXCITATION

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Background: Ventricular pre-excitation (VPE) is a conduction abnormality diagnosed on electrocardiogram. Risk assessment prior to sports participation is recommended because VPE can lead to sudden death secondary to rapid anterograde conduction down the accessory pathway during atrial fibrillation (AFib).

Objectives: To determine the ability of transesophageal electrophysiology studies (TEEPS) to assess risks of asymptomatic patients with VPE.

Methods: A retrospective review of patients with VPE who underwent TEEPS was performed. Inclusion criteria included age ≤18 years and no history of tachycardia or syncope. Data gathered included age, weight, height, congenital heart disease, sedation used, and TEEPS results. Patients were classified as having risk if the shortest pre-excited R-R interval during AFib was ≤250 ms, or no risk if it was >250 ms.

Results: Sixteen patients met inclusion criteria with an average age of 12.1 years, average height of 150 cm, and average weight of 49 kg. Standard TEEPS procedures were performed. AFib was induced in 12 (75%). Use of sedation (69%) vs. anesthesia (31%) had no effect on inducibility. TEEPS identified 19% of asymptomatic patients with risk of sudden death and 25% with supraventricular tachycardia. Additionally, TEEPS was significantly better at inducing AFib (12/16) than transvenous electrophysiology studies (97/212, $p=0.024$). No complications occurred.

Conclusions: TEEPS is an effective method for assessing risk in asymptomatic patients with VPE. AFib was inducible in the majority of patients. In those in whom AFib was noninducible, supraventricular tachycardia was induced. TEEPS is more effective that transvenous EPS at inducing AFib.

56 ACCESS TO HEALTH SERVICES AND ADHERENCE TO ANTIHYPERTENSIVE MEDICATIONS AMONG OLDER ADULTS

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57 DEPRESSION AND OLDER ADULTS: IMPACT OF DEPRESSIVE SYMPTOMS ON MEDICATION ADHERENCE

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Background: Little is known about the relationship between depressive symptoms, social support, and medication adherence for asymptomatic chronic diseases such as hypertension in older adults.

Objectives: We examined the associations between depressive symptoms, social support, and antihypertensive medication adherence in older adults.

Methods: We conducted a prospective cohort study of 2,180 community-dwelling older adults enrolled in a managed care organization and treated for hypertension. The Center for Epidemiologic Studies-Depression Scale (CES-D), the Medical Outcomes Study Social Support Index (MOS-SS), and the Morisky Medication Adherence Scale (MMAS-8) tools were administered at baseline and at 1 year follow-up. Medication possession ratios (MPR) were calculated using antihypertensive pharmacy fill data.

Results: The mean age of participants was 75 ± 5.6 years, 30.7% were black, 58.5% were women, 13% had depressive symptoms (CES-D ≥16), 33.9% had low social support (MOS-SS <75), and 14.1% had low antihypertensive medication adherence (MMAS-8 <6) at baseline. After multivariable adjustment, participants with depressive symptoms and those with low social support were 1.96 (95% CI 1.43, 2.70) and 1.27 (95% CI 0.98, 1.65) times more likely, respectively, to have low antihypertensive medication adherence by MMAS-8 and 1.52 (95% CI 1.14, 2.01) and 1.11 (95% CI 0.90, 1.37) times more likely, respectively, to have nonpersistent MPR at baseline.

Conclusions: Depressive symptoms may be an important modifiable barrier to antihypertensive medication adherence in older adults.

58 UNTANGLING THE ASSOCIATION BETWEEN ANTIHYPERTENSIVE MEDICATION ADHERENCE AND BLOOD PRESSURE CONTROL

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Background: The Cohort Study of Medication Adherence among Older Adults (CoSMO) is a prospective study of the barriers to antihypertensive medication adherence conducted among older adults with essential hypertension.

Objectives: Using data from CoSMO, we examined the relationship between medication adherence and blood pressure (BP) control and explored issues surrounding the use of blood pressure data obtained from electronic medical records (EMR) for epidemiological research.

Methods: Data were analyzed on patients who participated in the baseline survey and had at least one primary care visit with a BP reading in the year prior to their survey date (n=2,037). BP data were abstracted from clinical readings in Ochsner's EMR system. Adherence to antihypertensive medication was assessed with the self-report Morisky Medication Adherence Scale (MMAS-8) and the Medication Possession Ratio (MPR), constructed from pharmacy fill data.

Results: Substantial terminal digit and threshold bias was detected from BP readings. Prevalence of uncontrolled BP and low adherence by MMAS-8 and MPR was high among patients with only a single primary care (PCP) visit in the previous year (43.8%, 15.2%, and 28.8%, respectively) and among patients with six or more PCP visits (35.7%, 16.3%, and 32.9%, respectively). Associations between medication adherence and BP control were strongest for patients with six or more visits. These patients were also more likely to have other comorbidities ($p<0.001$) and to be filling three or more classes of antihypertensive medication ($p<0.001$).

Conclusions: The relationship between number of primary care visits, patient characteristics, and medication adherence is informative for understanding barriers to treating hypertension.

59 SELF-REPORTED ADHERENCE TO ANTIDIABETIC MEDICATIONS IS ASSOCIATED WITH GLYCEMIC CONTROL IN PATIENTS WITH TYPE 2 DIABETES

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60 HEALTH-RELATED QUALITY OF LIFE AND ANTIHYPERTENSIVE MEDICATION ADHERENCE AMONG OLDER ADULTS

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Background: Health-related quality of life (HRQOL) is an important psychosocial characteristic that may negatively impact an individual's ability to manage his or her chronic disease.

Objectives: To examine the association between measures of mental and physical HRQOL and antihypertensive medication adherence in older adults.

Methods: As part of a longitudinal cohort study of community-dwelling older adults enrolled in a managed care organization and treated for hypertension (n=2,180), Physical and Mental Component Summary (PCS and MCS) scores of HRQOL were assessed using the RAND Medical Outcomes Study 36-item tool. Adherence to antihypertensive medication was assessed with the 8-item Morisky Medication Adherence Scale (MMAS-8).

Results: The mean age of participants was 75 ± 5.6 years, 30.7% were black, 58.5% were women, 14.1% had low antihypertensive medication adherence (MMAS-8 scores <6), and one-third had low PCS and MCS scores. The multivariable adjusted odds ratio for low and medium, versus high, antihypertensive medication adherence associated with being in the lowest tertile of PCS scores was 1.37 (95% CI 1.12, 1.67, p=0.002) and 1.40 (95% CI 1.07, 1.83, p=0.015), respectively. The multivariable adjusted odds ratio for low and medium, versus high, antihypertensive medication adherence associated with being in the lowest tertile of MCS scores was 2.45, (95% CI 1.88, 3.19, p<0.001) and 1.62 (95% CI 1.32, 1.98, p <0.001), respectively.

Conclusions: Low HRQOL scores are associated with lower levels of antihypertensive medication adherence in older adults. HRQOL may be an important barrier to achieving high medication adherence.

61 RESULTS OF A PILOT PROGRAM AIMED AT IMPROVING HANDOFF TRANSITIONS AND PERCEPTIONS OF PATIENT SAFETY

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Background: The program was aimed at improving employee perceptions of patient safety and improving hand-off transitions. The organization had implemented an online occurrence reporting system at the beginning of 2009 and noticed a growing trend in the number of incidents submitted around care coordination (approximately 200% increase over two subsequent quarters). In addition, the organization conducted an employee patient safety culture assessment utilizing the Agency for Health Care Research and Quality (AHRQ) survey tool in 2009, scoring below the AHRQ average for several questions in category of "Handoff Transitions," which further supported the need for intervention.

Methods: The organization adapted and modified the "Patient Safety Friday" program from New York Presbyterian Hospital to fit the culture and the issues at Ochsner and used a newly created reporting system as a proxy measure for improvement.

The program consisted of weekly didactic meetings for mid-level managers during which an educational topic on patient safety would be presented. Also, mid-level managers were taught how to conduct patient safety walk rounds, and specific questions were crafted for use during these rounds to identify underlying process issues for care transitions. Findings were reported, and applicable follow-up was required.

Results: Qualitative results of the effort include the provision of data from across the system to leadership, the development of reports to support continued surveillance, increased verbal reporting of occurrences, and the ability to investigate incidents immediately.

62 RESOURCE UTILIZATION IN LIVER TRANSPLANTATION

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Background: Liver transplantation is among the most costly of surgical services, yet our understanding of the correlation between resources utilized and measures of risk is unknown.

Methods: We retrospectively reviewed a cohort of patients who received liver transplantation between January 1 and October 31, 2009. Resources utilized were derived from a charge database using a cost-to-charge ratio of 40%.

Results: Higher resource utilization was correlated with length of stay ($r^2=0.42$), cold ischemic time ($r^2=0.24$), Model for End-State Liver Disease (MELD) score ($r^2=0.19$), Scientific Registry of Transplant Recipients (SRTR) expected survival ($r^2=0.08$), MELD $\times$ donor age ($r^2=0.07$), and donor risk index ($r^2=0.09$).

Conclusions: We found considerable variation in the resources utilized for liver transplantation. Analysis suggests that the preoperative clinical characteristics most correlated with resource utilization were MELD score, SRTR expected survival, MELD $\times$ donor age, and donor risk index. Our results demonstrate the importance of cold ischemic time, and treating liver transplantation as anything other than an emergency is economically unwise. The principal mechanism through which clinical characteristics caused higher resource utilization was to increase the length of stay. It appears that significant savings might result from a reduction in variation.

63 EVALUATING THE IMPACT OF A 3-PHASE PROJECT ON SUSTAINING HAND HYGIENE COMPLIANCE ON A TRANSPLANT UNIT

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Background: More than 1.7 million patients develop a hospital-acquired infection (HAI) at a cost of $6.7 billion annually. Poor hygiene is a contributor to more than 270 HAI deaths each day.

Objectives: To evaluate the impact of a 3-phase project (Awareness, Feedback, and Sustain) on health care workers' hand hygiene compliance on a 34-bed unit.

Methods: Increasing awareness about hand hygiene was accomplished using educational strategies and posters. Audits of hand hygiene compliance were completed on a randomly selected day each week for a 12-month period. Feedback regarding individual compliance used different strategies for nurses (one-on-one) and physicians (group report). Outcomes included baseline and longitudinal compliance rates over 12 months. Chi-square analysis was used to test for differences in compliance between groups, and linear regression was used to identify variables impacting compliance sustainability.

Results: A total of 1,599 observations from 7 physicians and 42 nurses were collected. Baseline compliance was 67%, with 12-month improvement to 89%. Nurses were significantly more compliant than physicians, χ^2 (1, N=1,599)=28.5, $p<0.0001$. Time was a significant predictor of improved compliance: $\beta=0.14$, $t(1,598)=5.69$, $p<0.0001$. Nurse compliance explained a significant proportion of variance in compliance over time, $R^2=0.04$, $F(2, 1,598)=32.53$, $p<0.0001$.

Conclusions: Strategies focusing on awareness and direct feedback to both physicians and nurses were associated with early and sustained improvement in compliance. This 3-phase project provides valuable insight regarding how to improve hand hygiene compliance rates.

64 EVALUATING SAFETY OF HANDOFFS BETWEEN ANESTHESIA CARE PROVIDERS, PART II

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Background: Anesthesia care providers frequently exchange care of patients among one another. Few tools are available to them to ensure that the transfer of care happens without error. Addressing this concern, the Ochsner Anesthesiology Department developed a handoff menu that will be incorporated as a mandatory field on the electronic anesthesia record.

Methods: In 1–2 months' time, anesthesia care providers will be required to complete this menu when cases are being handed off between anesthesia providers. Surveys assessing the adequacy of patient care handoffs between anesthesia care providers have been distributed to all anesthesia staff, residents, and certified registered nurse anesthetists (CRNAs) in our department prior to implementation of this electronic protocol.

Results: Seventy-five completed surveys were received. Of those surveyed, 20% found the current handoff process to be inadequate, 84% reported receiving a poor/incomplete handoff in the prior year, 57% reported giving a poor handoff in the prior year, and 25% did relate an adverse outcome to a poor handoff. The overwhelming majority felt that standardization of this process could improve patient care. Most reported that ideal handoffs would occur both in the operating room and in person, and most agreed that handoffs should be incorporated into the electronic medical record.

Conclusions: After implementation of the new computerized handoff protocol, a similar survey will be distributed to the anesthesia staff, residents, and CRNAs in our department. Comparing the results from the two surveys will allow us to evaluate perceived changes in safety and quality of anesthetic practice since the inclusion of the handoff form in the electronic medical record. It is believed that a comparison of surveys will demonstrate a perceived improvement in handoff adequacy after implementation. Through this study, we aim to identify a handoff method that will help us decrease errors associated with handoffs, decrease complications, and improve patient safety.

65 INFECTION PREVENTION: THE OCHSNER MEDICAL CENTER–NEW ORLEANS EXPERIENCE

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Background: Bacteria, germs, viruses, mold, and other invisible pests pose a major threat to health care facilities. Infection prevention is an essential safety component to combat this problem. The Infection Control Department at Ochsner Medical Center–New Orleans serves in a general capacity to prevent the spread and acquisition of infectious agents. Briefly, the infection preventionist conducts surveillance activities, assesses quality care based on Infection Control metrics, and provides consultative services and education on infections and prevention measures to staff, patients, and visitors.

Methods: Infection Control reports data on preventable medical errors, including Class 1 surgical site infections, vascular catheter-associated bloodstream infections, catheter-associated urinary tract infections, and ventilator-associated pneumonia. Efforts to drive infections to zero include: real-time reporting of infections to the nursing units, physicians, and administration; meetings with physicians and nursing unit staff to develop and discuss prevention plans; education of employees and physicians about their part in preventing infections; and presentation of data to employees via the annual Skills Fair.

Results: In 2008, the facility experienced 57 Class I surgical site infections, 22 catheter-associated urinary tract infections, and 45 central vascular catheter-associated infections; there were 6 cases of ventilator-associated pneumonia from June through December 2008. In comparison, in 2009 there were 47 Class I surgical site infections, 28 catheter-associated urinary tract infections, 42 central vascular catheter-associated infections, and 25 cases of ventilator-associated pneumonias.

Conclusions: Active surveillance and data collection on preventable infections are ongoing. Incremental improvements have been achieved in most areas this past year compared to 2008. These Infection Control metrics are reported monthly via the Ochsner Health System organizational quality dashboard. Our efforts bring attention to infections and help drive infections toward zero.

66 IMPROVING HAND HYGIENE THROUGH INNOVATIVE SOLUTIONS

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Background: Hand hygiene is considered a best practice for infection prevention of contact-spread communicable diseases. Studies focused on hand hygiene show that on average health care workers wash their hands with soap and water or use alcohol-based sanitizers 40% of the time.

Objectives: To improve hand hygiene compliance using a multiphased approach.

Methods: We conduct hand hygiene audits monthly in a 500-bed hospital as well as ongoing education efforts. Individuals are given performance feedback on the spot. Hand hygiene signs are posted. Nurses are educated at Skills Fair and departmental meetings. We have encouraged unit-based hand hygiene performance improvement projects and provide compliance rates monthly. Units have created internal hand hygiene promotions. Innovative signage and symbols to promote adherence to hand sanitizing protocols have been developed. Camera surveillance has been conducted.

Results: Overall, our hand hygiene compliance was ≥40% for 11 of 12 months in 2009. Compliance rates were, chronologically, 80%, 41%, 22%, 75%, 51%, 55%, 51%, 65%, 53%, 69%, 65%, and 62%. Health care workers are aware of this patient safety initiative. Awareness is high, while compliance needs improvement.

Conclusions: Despite camera surveillance, our rates have not reached the expected target of ≥75%. A ''Call to Action'' from executive leadership is needed to help drive compliance toward the target.

67 PALLIATIVE CARE TEAM INITIATIVES IN CRITICAL CARE

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Background: Approximately 20% of all deaths in America occur in critical care units annually. Studies show that many physicians and nurses are uncomfortable discussing end-of-life issues with patients and providing palliative care to dying patients and their families.

Objectives: To evaluate ongoing satisfaction with contributions of the palliative care consultant service.

Methods: The Palliative Care team initiated a three-phase approach to address satisfaction:

- **Phase I**—Patient and Family Satisfaction: Press Ganey consultation to develop a bereavement survey to assess family satisfaction with end-of-life care.
- **Phase II**—Physician Training Satisfaction: A survey was developed and administered to residents at the beginning and end of their rotation on the Critical Care service to evaluate satisfaction with a new educational initiative.
- **Phase III**—Nursing Satisfaction: A pre- and postimplementation survey was used to evaluate nurses' perceptions of withdrawal of life support with and without a standardized order set.

Results:

- **Phase I**—Patient and Family Satisfaction: The pre-Palliative Care score was 76.7; it improved to 89.7 by April 2007. A 27% improvement in bereavement satisfaction was noted by 2009.
- **Phase II**—Physician Training Satisfaction: Resident confidence in providing palliative care improved, specifically, delivering bad news, discussing comfort care, withdrawing life-sustaining treatment, and managing dying patients.
- **Phase III**—Nursing Satisfaction: A strong positive linear correlation between years in nursing and comfort level with withdrawal of life support was noted relating to order sets. Many critical care nurses at OMC have less than 3 years' experience.

Conclusions: A 69% increase in palliative consults and a 27% increase in bereavement scores from 2008 to 2009 demonstrate ongoing satisfaction with the Palliative Care consultant service.

68 TRANSFORMING THE WORK ENVIRONMENT BY EXEMPLARY PROFESSIONAL PRACTICE

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Background: Professional development, staff retention, quality outcomes, and cultural change are common challenges in critical care.

Objectives: To create a structure to provide and sustain safe, efficient, and cost-effective care using the six pillars of a healthy work environment.

Methods: A multidisciplinary team addressed each pillar using specific strategies. True collaboration was addressed by clarification of physician expectations monthly and recognition of nurses as patient care coordinators. Effective decision-making involved data-driven decisions and implementation of best practices. Appropriate staffing matched nurse competencies with assignments. Orientation was restructured to include hands-on information, a phased approach to skill acquisition, and individual learning maps. Didactic and patient simulation improved clinical knowledge and critical thinking. Authentic leadership required strategies to generate enthusiasm, provide resources, share information, and appraise performance. Preceptors played a pivotal role in establishing relationships with 44 new hires on a 32-bed unit.

Results: Twelve-month outcomes included: improved RN satisfaction from 48% to 51%, turnover from 40% to 15%, vacancy from 29% to 17%, clinical ladder from 10% to 26%, and cost avoidance of $325K for 2009. Best practices such as sepsis management led to a 30% reduction in mortality, with an approximate annualized cost avoidance of $2 million.

Conclusions: This project created a healthy work environment for professional staff and positively impacted patient outcomes.

69 UNDERSTANDING FALL RISK FROM THE MEDICAL SURGICAL PATIENT'S PERSPECTIVE: A QUALITATIVE STUDY

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Background: Inpatient fall-related injuries remain a challenge for nursing. Falls lead to adverse outcomes: hospital injuries and increased cost. Adverse outcome reporting identified "instructions disregarded" as a major contributor for falls. Awareness of beliefs about health-related behaviors is essential to determine the effect beliefs have on behavior. Little is known about the impact on fall reduction of patients' perceptions about individual risk and their understanding of safety instructions.

Objectives: To uncover fundamental information about medical surgical patients' perceptions of fall risks and factors impacting risk for falling.

Methods: The sample included medical surgical patients hospitalized at a 540-bed tertiary teaching hospital. Open-ended interview questions were used to answer the research questions: Do patients perceive that they were informed of their individual fall risk? Can patients verbalize fall-related safety instructions? What factors impact their ability to wait for help? Redundancy was achieved with 37 subjects.

Results: Content analysis revealed three themes: nursing issues, patient's physical condition, and personality traits. Researchers discovered that most patient participants did not perceive that they were given adequate fall prevention instructions, some will never call for assistance regardless of instructions, and others will not wait more than 5 minutes for help.

Conclusions: These findings support a practice change that includes assessment of daily individual fall risk, understanding of and adherence to instructions, verbal/written reinforcement of instructions, and tolerance for waiting.

70 DRIVING IMPROVEMENTS IN SURGICAL CARE

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Background: According to the Institute for Healthcare Improvement's Surgical Care Improvement Project (SCIP) report, 30 million inpatient surgeries are performed every year in the United States; a "significant percentage result in preventable, often life-threatening complications." Antibiotic selection and timing are a SCIP measure that studies show will reduce infection-related complications.

Methods: Physician champions from Anesthesiology took ownership of the antibiotic appropriateness indicator. A Rapid Change group was assembled and collaborations formed. Processes were changed, including a redesign of the anesthesia record to prompt documentation. Surgery-based physicians were educated on the changes. SCIP data were reported to Surgery staff at Surgery Performance Improvement committee meetings and Surgery Council and to various medical and nursing leaders through the Performance Improvement committee.

Results: Data collection for antibiotic timing began first quarter 2006. Incremental improvements have been observed over time. Preoperative antibiotic timing compliance was as low as 40% in 2006. Rates rose in 2009: 76.5%, 80.2%, 83.9%, and 88.5% in quarters 1 through 4 to date, respectively. The compliance rate for antibiotic selection was as low as 89% in 2006. Rates have increased in 2009, with some fluctuations: 98.9%, 98.9%, 96.6%, and 89.3% in quarters 1 through 4 to date, respectively.

Conclusions: Antibiotic timing and selection are important SCIP indicators improving perioperative morbidity and mortality. Reaching a target compliance rate of 90% or better requires a collaborative effort among perioperative physicians, nurses, pharmacists, and Performance Improvement staff.

71 EVALUATING OUTCOMES OF ANTI-INCONTINENCE PROCEDURES: DEVELOPMENT OF A MAIL-BASED PAD KIT

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Background: Outcomes evaluation for the various treatments of stress urinary incontinence is often subjective, and a standard definition is lacking. Validated questionnaires exist, but an objective measure is usually difficult to obtain as it involves patient time and ancillary procedures.

Objectives: To assess the feasibility of a mail-based kit combining a 24-hour pad test and validated questionnaires in an attempt to evaluate objective and subjective endpoints as part of an overall incontinence outcomes assessment.

Methods: The mail-out pad kit was designed through collaboration with the institutional Biosafety Committee and the US Postal Service (USPS). The common mandate was to develop a leak-proof system that met federal and institutional requirements in four specific areas: specimen category, hazard class, risk group, and shipping class. 1. Specimen category: The pad kit is categorized as a diagnostic specimen. 2. Hazard class: The pad kit is designated as Class 6: Toxic Substance, Infectious Substance or Diagnostic Specimen. 3. Risk group: The risk in sending this kit via the mail was evaluated by the above parties and placed in Group 1, microorganisms unlikely to cause human or animal disease. This kit is not regulated as a hazardous material but is subject to the packing requirements of USPS code 601.10.17.10.4. Shipping class: The USPS requires a biohazard symbol along with a three-step packing procedure to ship Class 6 specimens as either First-Class, Priority, or Express Mail.

Results: Multistep packaging is required: First, the incontinence pad must be placed in a leak-proof primary receptacle (zip-top bag). Then that receptacle is placed in a leak-proof secondary vessel (biohazard bag). It must be able to withstand an internal pressure differential of no less than 95 kPa without leaking, as well as contain an absorbent sheet able take in all contained liquid in the event of a spill. Third, the sealed secondary vessel is placed into a strong container (corrugated 11 1/8″ × 8 3/4″ × 2″ box), which is then placed into an orange, moisture-proof, biohazard shipping envelope. The cost of the kit was under $2, and the cost for mailing the kit with return postage was $9.60. The above measures gained approval from the USPS and the institutional Biosafety Committee.

Conclusions: A mail-based pad test kit is feasible and can be administered with local Institutional Review Board approval using the above guidelines. This protocol can be utilized by any practice desiring a balanced measure of outcomes.

72 IMPLEMENTING A NEW PROFESSIONAL NURSING MODEL OF CARE

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Background: The Ochsner Health System Nursing Department sought to integrate a professional practice model (PPM) based on relationship-based care (RBC).

Objectives: To implement a new PPM to improve selected structural and process outcomes.

Methods: The Caring Model™ (I.C.A.R.E.) was used as a first step to change to RBC. I.C.A.R.E. includes the following steps: Introduce yourself to the patient. Call the patient by preferred name. Use appropriate touch. Review the plan of care while sitting at the bedside, for 5 minutes. Every time care is provided, keep our mission in mind.

Education on RBC, I.C.A.R.E., and Swanson's caring theory was provided to the nursing staff in May. Data were collected pre- and postimplementation. The study used a convenience sample on the Medical-Surgical units along with a random sample of patient discharges through Press Ganey.

Results: Patient satisfaction for overall nursing care for April was 86.6%; postimplementation, it increased to 87.6%. Although other efforts surround patient satisfaction, I.C.A.R.E. targeted the nurse-patient relationship, making this slight improvement a positive trend. The Nurses' Perception survey comparing pre- to postintervention scores revealed no significant changes overall; however, the indicator for "Being With" showed an increase that approached significance ($\chi 2=11.2$, $p=0.47$). This indicator is a reflection of "R" in I.C.A.R.E.

Conclusions: Changing the PPM is a multiyear process that incorporates a change in culture. Positive trends were identified and need to be studied over a longer period of time.

C1 ACUTE PAIN MANAGEMENT IN A PEDIATRIC PATIENT FOLLOWING REPTILE LIMB AMPUTATION

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Introduction: Pediatric acute pain management can be difficult, especially after a traumatic event. Opioid analgesics are the mainstay of prescribed medications for acute pain by many surgical services. Here we present an interesting acute pain management scenario involving a traumatic amputation of the patient's entire arm.

Case Report: A 12-year-old was swimming in a bayou in southeast Louisiana. A large alligator, known to inhabit this bayou, attacked the child. The reptile disarticulated the left upper extremity. The patient was immediately rescued and transferred to our facility. Postoperatively, the patient's pain was not controlled. Dressing changes required general anesthesia. On postoperative day 3, the acute pain service was consulted; following an assessment, an interscalene catheter was recommended. Under general anesthesia using sterile technique, a 20-gauge polyurethane catheter was inserted into the interscalene nerve sheath. On post-catheter insertion (POC) day 1, the patient reported his pain as 1/10. On POC day 2, the patient tolerated an awake dressing change. Pregabalin, 50 mg orally twice a day, was used to help with the onset of neuropathic pain. The previously started intravenous narcotics were discontinued, and the patient was slowly transitioned to oral pain medications. The catheter was discontinued on POC day 5. On POC day 6, the patient was discharged to home on pregabalin and acetaminophen with outpatient rehabilitation.

Discussion: The use of interscalene catheters placed under ultrasound is not new for postoperative pain in the pediatric population. Case reports describe the use of interscalene catheters in children for cancer pain and following postsurgical amputation. Also, the use of perineural catheters has recently been described after traumatic injuries in adults serving in the Iraq war. However, this is the first known reported case of the use of an interscalene catheter after traumatic amputation on a pediatric patient.

C2 ACUTE CEREBRAL ANGIITIS WITH THALAMIC STROKE ASSOCIATED WITH HERPES ZOSTER OPHTHALMICUS

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Introduction: Herpes zoster typically presents with self-limiting vesicular rash and neuropathic pain. In rare cases, herpes zoster ophthalmicus-associated cerebral angiitis can develop and lead to cerebral infarction.

Case Report: A 74-year-old male with a history of hypertension and chronic atrial fibrillation on warfarin presented with acute left-sided dysmetria and gait difficulty. Ten days prior, he developed right trigeminal herpes zoster involving the ophthalmic branch and was treated with oral valacyclovir and gabapentin. Vital signs at physical examination were temperature: 98°F; blood pressure: 140/90 mmHg; and pulse: 74 beats/min. He had left facial droop, decreased sensation to pin prick of his left face and lower extremity, and gait instability. His prothrombin time-international normalized ratio was therapeutic. Brain magnetic resonance imaging revealed a <1 cm acute infarct in the right thalamus and no major cerebral vessel occlusion. Analysis of the cerebrospinal fluid (CSF) showed glucose of 73 mg/dL, protein of 79 mg/dL, and white blood cell count of 19/CuMm with 98% lymphocytes. Further evaluation of the CSF by polymerase chain reaction demonstrated the presence of herpes zoster of 1:8. Dexamethasone and aspirin were started for probable herpes zoster-associated small vessel cerebral angiitis. Valacyclovir and gabapentin were continued. His condition rapidly improved after 3 days of treatment.

Discussion: Cerebral angiitis has recently been reported in patients with trigeminal herpes zoster. Aberrant central nervous system immune response from the infection results in inflammation and destruction of isolated small cerebral arteries. Arterial thrombosis may follow, leading to stroke. Cerebral angiitis has been reported to mimic and trigger ischemic stroke. A distinction can be difficult to make clinically, especially if the patient has risk factors for ischemic stroke. Small vessel involvement may not be evident on imaging studies, as in this case. Failure to recognize this entity early may lead to worsening neurologic progression due to continued vessel inflammation. Current treatment is based on anecdotal reports of successful antiviral therapy as well inflammation reduction with tapered corticosteroid doses until neurologic symptoms are stable.

C3 DELAYED ONSET POST-TRANSPLANT LYMPHOPROLIFERATIVE DISORDERS IN POST-MULTIORGAN TRANSPLANT PATIENTS

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Introduction: Post-transplant lymphoproliferative disorders (PTLD) commonly present within the first year post-transplant with incidence declining precipitously thereafter. Incidence of and mean time to develop PTLD lessen as immunosuppression intensity increases. The highest rate has been reported among multiorgan transplant patients.

Case Report: A 32-year-old female—16 years after bilateral lung transplantation secondary to cystic fibrosis and 7 years after kidney transplantation following end-stage renal disease from cyclosporine toxicity—presented with intermittent nausea, vomiting, 11-lb weight loss over 2 months, and colicky abdominal pain with tenderness. Her laboratory tests showed anemia and elevated low-density lipoprotein cholesterol of 1,053 U/L. Polymerase chain reaction testing revealed Epstein-Barr virus (EBV) DNA of 4,500 copies. Noncontrast computed tomography (CT) showed a large soft-tissue mass in the distal jejunum and multiple masses in the kidneys, liver, and pancreas. They were hypermetabolic by positron emission tomography imaging, which also showed a soft-tissue lesion in the left breast. Biopsy showed diffuse large B cell lymphoma and a negative stain for EBV.

Discussion: Chronic immunosuppression with tacrolimus was discontinued, and single-agent rituximab started. Despite hydration and prophylactic rasburicase, she developed tumor lysis syndrome. Prior to the third cycle, her symptoms worsened and a repeat CT scan revealed disease progression of the masses. Cytotoxic chemotherapy with cyclophosphamide, doxorubicin, vincristine, and prednisone was added to the rituximab. Despite her severe tumor lysis syndrome, which required renal replacement therapy, she has shown significant clinical improvement after two cycles of chemotherapy.

PTLD is an uncommon, though serious, complication of chronic immunosuppression in post-solid organ transplant patients. It is typically of B cell origin and is known to be induced by EBV infection. Its overall incidence in the general transplant population is about 1%, with a higher risk among patients receiving more intense immunosuppression (typically within the first year after transplant) and post-multiorgan transplant patients. Other documented risks include chronic exposure to tacrolimus, age younger than 25 years, history of pre-transplant malignancy, and being EBV seronegative pre-transplant. Prevention involves limiting aggressive immunosuppressants, rapidly withdrawing or tapering such agents, and using anti-viral prophylaxis. Regarding treatment, current data favor a regimen that first reduces immunosuppression and then uses single-agent rituximab or combined chemotherapy. Rituximab has induced complete remission in some patients but carries a risk of tumor lysis syndrome; pre-treatment caution is advised. Surgery and radiation have been curative in disease involving focal lesions. The prognosis of PTLD is generally poor, with overall survival rates ranging from 25%–30%.

C4 ALL THAT GLITTERS IS NOT GUILLAIN-BARRE: A SPINAL ABSCESS CAUSING ASCENDING PARALYSIS

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Introduction: Spinal epidural abscess (SEA) is a rare infection in patients under the age of 50 with no history of intravenous drug use or epidural catheter placement. Incidence ranges from 2 to 25 patients per 100,000 admissions and has been increasing over the past 30 years. SEA is a severe infection that requires prompt recognition and management to avoid potentially disastrous complications.

Case Report: A 44-year-old male with hypertension and diabetes presented with sudden onset of bilateral lower extremity weakness that started 10 hours prior to admission. His lower legs had become weak and gave out on him while changing clothes. He recovered seconds later, but his weakness returned and he eventually became paralyzed. After a lumbar puncture, his upper extremities became weak, and he had difficulty urinating. He also complained of an occipital headache (5/10) that was worse with flexion. Vital signs were within normal limits. Light touch sensation and vibration on the dorsal surface of the feet were absent. Strength in the lower extremities was 0/5, and strength in the upper extremities was 3/5. His lower extremities reflexes were absent bilaterally, and a positive Babinski's sign was elicited. White blood cell count was 11.5 K/uL. Metabolic profile, urinalysis, influenza screen, troponin, electrocardiogram, and computed tomography of the head and spine were normal. C-reactive protein was 150.3 mg/L, and myoglobin was elevated at 267.6 g/dL. The cerebrospinal fluid was slightly xanthochromic, and results showed white blood cells=7/CuMm, glucose=58 mg/dL, red blood cells=1/CuMm, and protein=452 mg/dL. Suspicious of possible neck injury, magnetic resonance imaging (MRI) and angiography of the head and neck were ordered. While waiting for the results, blood pressure dropped to 74/48 mmHg, and the patient was intubated for respiratory failure. Intravenous immunoglobin was ordered initially to treat for Guillain-Barre syndrome.

However, cervical MRI showed a collection of fluid anterior to the spinal cord between C3 and C6. The patient was transferred to the operating room for corpectomy and diskectomy with decompression and irrigation with vancomycin saline. The disks were cultured and grew *Streptococcus agalactiae* and *Staphylococcus aureus*, which were the same organisms found in a small (1×0.5 cm) superficial ulceration on his left foot. The patient was started on vancomycin for 6 weeks, along with physical therapy. His neurological deficit improved slowly.

Discussion: Spinal epidural abscess can be difficult to recognize, especially when symptoms coincide with other neurological diseases such as Guillain-Barre. Diagnosis must be made promptly because delay in surgical decompression or antibiotics may result in irreversible neurologic damage or death. Even though fever, malaise, and back pain are the most consistent early symptoms, patients can present with acute severe neurological symptoms, such as paralysis. MRI with gadolinium should not be delayed if epidural abscess is suspected.

C5 EFALIZUMAB-INDUCED INFLAMMATORY POLYARTHRITIS: WHAT ARE THE IMPLICATIONS?

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Introduction: Efalizumab is a monoclonal antibody that has been successfully used to treat psoriasis. The monoclonal antibody binds to the T cell surface integrin, LFA-1, thereby blocking its interaction with the intercellular adhesion molecule ICAM-1 on the surface of antigen-presenting cells and endothelial cells. This mechanism is thought to prevent T cell activation and migration into inflamed tissues with resulting clinical improvement of psoriatic skin disease.

Case Report: A 49-year-old female started efalizumab for severe psoriasis. Three weeks later, she developed rapidly progressive inflammatory polyarthritis associated with high titers of both rheumatoid factor (RF) and anti-cyclic citrullinated peptide (anti-CCP) antibody.

Discussion: Initial studies examining the therapeutic potential of efalizumab in psoriatic arthritis (PsA) were disappointing, as arthritis worsened in many of the cases. Furthermore, efalizumab has been shown to precipitate new onset PsA in some psoriasis patients. To our knowledge, this is the first reported case of efalizumab-induced anti-CCP-positive rheumatoid arthritis (RA).

Except for the presence of a rash, the polyarticular form of PsA is often indistinguishable from RA clinically. Furthermore, both diseases are associated with the shared epitope allele, indicating a possible common mechanism of disease. CD4 T cells play a prominent role in the pathogenesis of both RA and PsA. Efalizumab theoretically modulates that role and appears to precipitate inflammatory arthritis in susceptible patients.

Further research is needed to determine the exact relationship between efalizumab and inflammatory arthritis, as well as to further explore the apparent connection between the inflammatory polyarticular form of PsA and RA.

C6 IS IT A HEART ATTACK OR A FUNGUS? ANGIOINVASIVE ASPERGILLOSIS PRESENTING AS ACUTE MYOCARDIAL INFARCTION

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Introduction: In cirrhotic patients, the differential diagnosis for chest pain should include common etiologies but should also be broadened to include rare conditions, which are more frequently seen in this population.

Case Report: A 47-year-old African-American male with past medical history of alcohol-induced hepatic cirrhosis presented with acute mid-sternal chest pain of 5 hours' duration. Respiratory distress developed on presentation, and mechanical ventilation was required for airway protection. Initial work-up showed markedly elevated cardiac enzymes with creatine phosphokinase of 14,000 U/L, elevated aspartate transaminase of 800 U/L, alanine transaminase of 210 U/L, total bilirubin of 8 mg/dL, direct bilirubin of 7 mg/dL, and ST segment elevation on inferior EKG leads. The patient underwent emergent left heart catheterization, which revealed patent coronary arteries. Subsequently, multi-organ failure resulted in decompensated shock; several vasopressors were needed to maintain adequate vital organ perfusion. Blood, spinal fluid, urine, and sputum cultures showed no growth. Blood and urine toxicology screen was negative for substance abuse. Serology tests were negative for HIV, acute viral hepatitis, syphilis, dengue fever, tularemia, herpes virus 1 and 2, cytomegalovirus, Epstein-Barr virus, leptospirosis, Q fever, Lyme disease, brucellosis, and ehrlichiosis. The patient experienced an intractable ventricular fibrillation, which resulted in death after a 13-day hospital stay. Autopsy report confirmed disseminated angioinvasive aspergillosis involving heart, lungs, bowel, thyroid, kidneys, and spleen in addition to complete occlusion of the posterior descending artery with a fungal thrombus and multiple fungal endocardial vegetations.

Discussion: *Aspergillus* organisms are ubiquitous, and exposure to their conidia must be a frequent event. However, disease due to tissue invasion with these fungi is uncommon and occurs primarily in the setting of immunosuppression. Risk factors for invasive aspergillosis include prolonged and severe neutropenia, hematopoietic stem cell and solid organ transplantation, advanced AIDS, chronic granulomatous disease, and rarely cirrhosis. As is seen with other fungal infections, neutropenia and corticosteroid use are the most common predisposing factors. The most common manifestations of invasive aspergillosis involve the lung, upper airways, and contiguous structures. Infection may disseminate beyond the respiratory tract in patients who are seriously immunocompromised, such as those on corticosteroids or stem cell transplant recipients. Infection of virtually any organ can occur, but most commonly the kidney, liver, spleen, and central nervous system are involved. *Aspergillus* is second only to candida as a cause of fungal endocarditis. Septic embolization has been occasionally reported as a reason for cerebral, myocardial, and pulmonary infarctions in patients with malignancies, bone marrow transplant, aplastic anemia, and lung transplant. Our report represents another rare case of myocardial infarction due to *Aspergillus* septic emboli in the setting of hepatic cirrhosis.

C7 TREATMENT OF CORNEAL INTRAEPITHELIAL NEOPLASIA WITH INTERFERON THERAPY

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Case Report: The goal of the project was to evaluate interferon as an alternative treatment modality in limbal and corneal malignancies. Patient records from January 2005 to January 2010 were retrospectively reviewed, with the records of those patients who underwent interferon treatment (n=3) reviewed for outcomes. We determined that interferon treatment resulted in corneal clearing and long-term remission in these patients with corneal intraepithelial neoplasia.

C8 ABDOMINAL PAIN FROM ALLERGIES?

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Introduction: In young patients with a history of hypersensitivity reactions, the differential diagnosis for abdominal pain should include common etiologies but should also be broadened to include rare conditions that are more frequently seen in this population.

Case Report: A 30-year-old African-American male with multiple hypersensitivity reactions that required Emergency Department visits presented with a 2-week history of sharp, left lower quadrant abdominal pain with radiation toward the back along with a 1-week history of diarrhea with three episodes of hematochezia over the prior day. Initial work-up showed a leukocytosis of 16,000 with 44% eosinophils. Computed tomography of the abdomen revealed diffuse colonic and terminal ileum bowel wall thickening. Colonoscopy revealed slight granularity in the cecum and erythematous mucosa and diverticulosis in the sigmoid colon. Pathology revealed intense eosinophil infiltration in the terminal ileum, cecum, and descending colon. Stool studies were negative for *Clostridium difficile*, enterohemorrhagic *Escherichia coli*, shigella toxin, salmonella, vibrio, yersenia, and campylobacter.

Discussion: Eosinophilic gastroenteritis is an uncommon gastrointestinal disease, affecting both children and adults. Eosinophilic gastroenteritis is characterized by the presence of abnormal gastrointestinal symptoms, including abdominal pain, eosinophilic infiltration in one or more areas of the gastrointestinal tract, and 20 or more eosinophils per high-power field in the absence of an identified cause of eosinophilia. The exclusion of eosinophilic involvement in organs other than the gastrointestinal tract and a history of atopy or food allergies are often present. This represents another rare case of abdominal pain in the setting of eosinophilic gastroenteritis.

C9 THE RISE OF RHIZOPUS

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Introduction: As of 2007, 23.6 million people in the United States have a diagnosis of diabetes mellitus. Poorly controlled diabetes can predispose patients to several opportunistic infections. Of those included, mucormycosis is a rare but frequently fatal disease that requires aggressive surgical and antifungal treatment.

Case Report: A 21-year-old male with a past medical history of uncontrolled diabetes mellitus type 1 and intravenous heroin abuse presented with 3 days of constant, crampy abdominal pain starting in the right flank and upper quadrant, which progressed to diffuse abdominal pain. On physical examination, the patient had a pulse of 109 beats/min, with moderate diffuse upper quadrant tenderness to palpation. He had an elevated white blood cell count of 15.24 K/uL, and was initially placed on broad spectrum antibiotics via sepsis protocol. Diabetic ketoacidosis was diagnosed following the initial work-up, revealing an elevated glucose of 361 mg/dL, bicarbonate of <5 mEq/L, and an anion gap of 23. Urine analysis showed >1,000 mg/dL glucose and >80 mg/dL ketones. Computed tomography (CT) scan and renal ultrasound showed three focal parenchymal abscesses within the right kidney.

Using CT guidance, 2 cc of a thick greenish material was drained from an abscess located in the posterior aspect of the right kidney. Material was sent for Gram stain, culture, and sensitivities, which revealed *Rhizopus* species. Broad spectrum antibiotics were discontinued and replaced with intravenous amphotericin B and oral posaconazole. Following 1 week of therapy, repeat CT of the abdomen and pelvis revealed an increase in size of the three previously identified abscesses. With the increase in size of his lesions despite antifungal therapy, an uncomplicated right nephrectomy was performed. Patient was then discharged home with a 6-week course of intravenous amphotericin B.

Discussion: Mucormycosis is caused by a class of fungi that can cause a variety of infections in humans, particularly in immunocompromised patients, those with diabetes mellitus, and intravenous drug users. Diabetes mellitus has been reported in approximately 36% of the reported cases of mucormycosis since 1940, making it the most common risk factor. Ketone reductase, an enzyme found in *Rhizopus* organisms, allows them to thrive in high-glucose, acidic conditions. The infection can involve the lungs, central nervous system, gastrointestinal tract, and skin, but it is probably best known for its rhinocerebral presentation. Isolated involvement of the kidneys with mucormycosis has been reported and is thought to occur via seeding of the kidneys during an episode of fungemia. Most patients with isolated involvement have risk factors for fungemia, including intravenous drug use, AIDS, or intravenous catheter use. Treatment of mucormycosis involves a combination of surgical debridement of involved tissues and antifungal therapy.

C10 THE BONY TRUTH: VASCULAR CALCIFICATION IN CHRONIC KIDNEY DISEASE

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Introduction: There is an epidemic of chronic kidney disease (CKD) stages 3–5, affecting 16.5 million people in the United States. Cardiovascular disease (CVD) is responsible for approximately half of the deaths in patients with end-stage renal disease (ESRD). Vascular calcification is thought to be a significant contributor in the pathogenesis of CVD in CKD patients.

Case Report: A 37-year-old female with ESRD on dialysis and a history of chronic abdominal pain presented to the Emergency Department with acute worsening of her symptoms. Physical examination revealed abdominal tenderness to palpation. Abdominal noncontrast computed tomography showed portal venous gas and pneumatosis intestinalis along with extensive vascular calcifications throughout the entire arterial tree. Based on these findings, the decision was made to perform exploratory laparotomy, which revealed necrotic bowel. A diagnosis of mesenteric ischemia was made.

Discussion: Vascular calcification is a likely cause of cardiovascular morbidity and mortality in patients with CKD. In fact, aortic stiffness has been proposed to be used as a predictor of cardiovascular events. Evidence suggests that proteins involved in bone metabolism may transform vascular smooth muscle cells into chondrocytes or osteoblast-like cells. These changes result in the calcification of the arterial medial wall throughout the arterial tree. The decreased compliance of the vessels causes a maladaptive vascular bed that leads to a variety of cardiovascular events. This case is relevant because timely management of CKD patients can make a difference in the patients' outcome.

C11 A DISEASE IN NO MAN'S LAND

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Introduction: Idiopathic retroperitoneal fibrosis, considered a rare disease, is usually diagnosed once there is significant organ involvement (most commonly the kidney). Its vague insidious presentation is a challenge in establishing the diagnosis.

Case Report: A 57-year-old African-American male presented with chronic dull lower abdominal and back pain and recent urinary frequency with decreased urine output. He was found to be in acute renal failure with a creatinine of 12.6 mg/dL. Computed tomography (CT) of the abdomen revealed a retroperitoneal mass and significant hydronephrosis. He underwent emergent cystoscopy with double-J ureteral stent placement. On further review, it was noted that an abdominal CT scan 4 months earlier had revealed peri-aortitis. Evaluation by vascular surgery was negative for inflammatory aortic aneurysm, and no further intervention was performed. Fine needle aspiration of the retroperitoneal mass was negative for malignancy but revealed mixed inflammatory fibrous tissue, consistent with retroperitoneal fibrosis. He was started on prednisone 60 mg daily, with improvement of his abdominal and back pain. Three weeks later, his creatinine was back to baseline; his erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were both normal.

Discussion: Retroperitoneal fibrosis is mostly idiopathic but can be secondary to drugs, infection, malignancies, radiotherapy, or surgery. The pathogenesis is possibly secondary to an exaggerated local inflammatory reaction to aortic atherosclerosis or is a manifestation of the systemic autoimmune process. It presents insidiously with nonspecific systemic symptoms and is characterized by inflammation and peri-aortic fibrosis. Poorly localized low back and abdominal pain, anorexia, malaise, claudication, lower extremity edema, and testicular pain are associated symptoms. Usually, the diagnosis is not considered until the patient develops obstructive uropathy and renal insufficiency. Contrast-enhanced CT scan is the diagnostic study of choice as it allows visualization of the extent of fibrosis and presence of lymphadenopathy. Biopsy is often necessary to exclude malignancy or infectious etiology. Initial surgical treatment of the local mechanical complications is followed by long-term corticosteroid therapy. In refractory cases, immunosuppressive drugs such as azathioprine, methotrexate, cyclophosphamide, tamoxifen, or mycophenolate may be used. Response to therapy is monitored by ESR, CRP, and CT scan. The prognosis both for survival and long-term disease control is generally good with early diagnosis and treatment. Patients need indefinite surveillance for recurrence.

C12 IT'S IN THE FEVER: FEVER OF UNKNOWN ORIGIN AS AN ATYPICAL PRESENTATION OF SARCOIDOSIS

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Introduction: The list of etiologies of fever of unknown origin (FUO) is extensive, and it is an uncommon first presentation of sarcoidosis.

Case Report: A 54-year-old woman with a history of rheumatoid arthritis presented with fever, abdominal pain, and weakness at an outside hospital. After persistent high-grade fevers for 7 days, elevated liver function tests, and an abnormal ultrasound (thickened gallbladder with nonspecific pericholecystic fluid), she was transferred to Ochsner. At our hospital, she was evaluated by surgeons and underwent a cholecystectomy for acalculous cholecystitis, after which her abdominal pain resolved but she continued to have high-grade fevers despite antibiotics. She also had elevated alkaline phosphatase, peaking in the 700s (U/L) but with no evidence of obstruction. Extensive infectious disease work-up was negative; therefore, antibiotics were discontinued. A computed tomography scan was inconclusive, and a gallium scan showed abnormal uptake in the lungs, but pulmonologists felt this was unlikely to be the source of infection. No autoimmune or drug-induced etiology was found. A liver biopsy showed noncaseating granulomas; therefore, in the context of the clinical picture the patient was diagnosed with sarcoidosis. She was started on prednisone and followed up with her rheumatologist. Her fevers resolved, and her fatigue and weakness improved.

Discussion: Sarcoidosis typically presents with symptoms involving the lung or is found incidentally on chest radiograph; however, systemic symptoms such as fever can be the initial presentation. It is therefore important to keep sarcoidosis in mind in the evaluation of FUO to ensure rapid diagnosis and subsequent treatment.

C13 CHONDROID HAMARTOMA OF THE CERVICAL SPINE IN AN INFANT: A CASE REPORT

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Introduction: Chondroid hamartoma (CH) is a relatively rare benign tumor that most often presents as pulmonary lesions. It has been reported to occur at various locations along the respiratory tract, such as the trachea and nasopharynx. We describe the first known case of chondroid hamartoma in a cervical spinal mass with cord compression in an infant.

Case Report: A 10-week-old male presented with spastic quadriparesis. Computed tomography/magnetic resonance imaging showed a large dumbbell-shaped enhancing lesion involving the cervical spine and neck. The lesion was treated via two-staged surgical approach: 1) posterior C3–C7 laminoplasty with intraspinal tumor resection and foraminotomy followed by 2) anterior neck dissection with paraspinal tumor resection. The histopathology confirmed chondroid hamartoma. The patient did not receive any adjuvant therapy and was doing well at 9 months' follow-up.

Discussion: Awareness of this rare entity is important to pediatricians and pediatric neurosurgeons.

C14 LONG-TERM ALENDRONATE THERAPY AND SUBTROCHANTERIC FEMORAL FRACTURES

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Case Report: A 69-year-old woman experienced subtrochanteric fracture of her right femur. She was walking into her house when she tripped and fell forward. She was seen at the Emergency Department, where she was diagnosed as having subtrochanteric femoral fracture. She underwent intramedullary rod placement. Radiographs further revealed a nondisplaced subtrochanteric stress fracture of the left femur. She had been experiencing thigh pain 3 to 4 months before the fracture; she had had a fracture in the left fifth metatarsal about 1½ years previously, which was slow healing. She had been taking alendronate sodium for more than 7 years. The bone mineral density of her total hip (T score) had improved to −1.3 from −2.3 the previous year. Her 25-hydroxyvitamin D level was normal at 50 ng/mL (to convert 25-hydroxyvitamin D level to nanomoles per liter, multiply by 2.496). She had had no exposure to corticosteroids. Alendronate was stopped, and teriparatide was started.

Discussion: Alendronate reduces osteoclastic bone resorption and thereby increases bone mineral density and decreases bone turnover. Microdamage that occurs regularly in bone but is normally repaired may accumulate because of prolonged suppression of bone turnover by alendronate. This can result in the formation of stress fractures in areas of great loading such as the subtrochanteric region of the femur and the fifth metatarsal. Long-term alendronate therapy may cause completion and displacement of stress fractures, with low-energy insults and delayed healing likely because of oversuppression of bone turnover. In such cases, discontinuation of alendronate should strongly be considered. After diagnosing stress fracture, some clinicians suggest prophylactic rod placement to prevent a completed fracture or treatment with teriparatide. Teriparatide promotes the activity of osteoblasts, stimulates bone formation, increases bone mass, and improves bone microarchitecture.

C15 SCIATIC NERVE PALSY SECONDARY TO COMPRESSION BY HETEROTOPIC OSSIFICATION

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Introduction: Sciatic nerve entrapment due to heterotopic osseous formation is rare and has been reported four times in the past in orthopedic/trauma/rehabilitation medicine journals but only one case has appeared in a neurosurgical journal.

Case Report: We present a patient who developed lumbar radiculopathy from heterotopic ossification after surgically repaired pelvic fracture. After the confirmation of diagnosis by electromyography/nerve conduction study (EMG/NCS), neuroplasty/neurolysis along with excision of heterotopic bone formation that was encasing the sciatic nerve at the thigh was performed. This patient underwent local radiation and indomethacin treatment.

Discussion: The cases reported earlier are different from acute sciatic nerve compression directly from displacement and/or avulsion of adjacent normal bony structure. The onset of symptoms among these reported cases ranges from 6 weeks to 27 years. Unfortunately, the patient in this case report was seen by a peripheral nerve neurosurgeon several years after he had developed the symptoms, which may negatively influence his surgical outcome with regard to motor and sensory function.

Patients with sciatic/peroneal neuropathy with a distant history of trauma/orthopedic surgery in the adjacent bones need to be investigated carefully with proper work-up, especially when there is a negative spine magnetic resonance imaging (MRI) scan or even a minor degree of spine pathology demonstrated on MRI that is unlikely to be an etiology of patients' signs and symptoms. In these cases, EMG/NCS studies would be vital to localizing the level of injury and treating appropriately.

C16 VENTRICULAR FIBRILLATION IN A PATIENT WITH POMPE DISEASE: A CAUTIONARY TALE

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Introduction: Pompe disease is a rare autosomal recessive genetic disorder resulting from a deficiency of the acid α-glucosidase (GAA) enzyme. A lack of GAA results in the accumulation and deposition of glycogen in cardiac muscle, leading to hypertrophic cardiomyopathy and arrhythmias. We report a patient with Pompe disease who experienced ventricular fibrillation while under general anesthesia.

Case Report: The patient was a 3-month-old female who presented with respiratory distress. Her physical examination was remarkable for a large tongue, dysmorphic facies, hypotonia, and a grade II/VI systolic crescendo-decrescendo murmur. A chest radiograph demonstrated marked cardiomegaly, and an electrocardiogram revealed a shortened PR interval and left ventricular hypertrophy with strain. An echocardiogram showed concentric hypertrophic cardiomyopathy. Genetic testing resulted in a diagnosis of Pompe disease. General anesthesia with sevoflurane and vecuronium was used for implantation of a central venous line. Her heart rhythm rapidly deteriorated into ventricular fibrillation. She was successfully converted back to sinus rhythm with a 10 joule asynchronous electrical shock. The line was placed without further complications.

Discussion: Clinicians must be aware that when cardiomegaly is observed in an infant, Pompe disease should be included in the differential diagnosis. The known complication of arrhythmias associated with the use of general anesthesia should not be overlooked, and local anesthesia should be used whenever possible. If general anesthesia is determined to be clinically indicated, anesthetists should be carefully selected to maintain coronary perfusion and systemic vascular resistance. In addition, clinicians must be prepared to resuscitate these patients should complications arise.

C17 COSTELLO SYNDROME: LARYNGEAL MASK AIRWAYS DO NOT RELIEVE ALL CASES OF GLOSSOPTOSIS

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Introduction: Costello syndrome is characterized by mental retardation, coarse facies, redundant skin, papilloma, and poor post-natal growth. Costello syndrome was originally described in the 1970s and is considered a potentially difficult airway due to the following features: a short neck, presence of macroglossia, hypertrophied tonsillar and supraglottic tissues, laryngeal papilloma, and choanal atresia. A number of clinical reports of difficult intubation and of cardiac arrest have been published in patients with this syndrome. Reports of successful airway management with placement of laryngeal mask airways (LMAs) in patients with glossoptosis have been reported.

Case Report: In this case, we were unable to provide a patent airway with a selection of LMAs designed for infant care. We present a different and interesting management of a known difficult airway during left heart catheterization in an infant with a diagnosis of Costello syndrome who developed glossoptosis during inhalation induction of general anesthesia, in which infant-specific LMAs were unable to relieve the airway obstruction.