Musicogenic seizures are an extremely rare and complex form of reflex epilepsy, with only a few cases reported in the literature. We present the case of a 26 year old right handed female, a piano performance graduate student, who began experiencing spells in October 2001. She presents to the University of Michigan Comprehensive Epilepsy Program in February 2005 for evaluation, describing three semiologies. Her mildest spell is described as an auditory aura of either a distorted radio in the background or piano music with distorted human voices followed by slight confusion. The second type of spell begins in the same manner, then progresses to include a sense of being in another place, an inability to speak, and a more prolonged confusion. The most severe type of spell then progresses to a secondarily generalized convulsion.

She reports that her spells only occur while she either hears or plays piano music. On further questioning, she admits that spells can also occur if she is reading piano sheet music and hearing the melody in [her] head. She hears and plays piano music every day as a part of her graduate studies, and since the onset of her spells, she experiences auras with the piano music of various genres and composers. The spells are specific to the piano, both standard and synthesizer, and do not occur in the absence of piano music. General neurological examination, routine EEG, and Brain MRI with temporal lobe epilepsy protocol are normal. Long term monitoring by video and EEG captured a typical spell with secondary generalization while the patient played a keyboard at her bedside. The musical piece was Bach's Goldberg Variations, a previously identified trigger. The ictal EEG reveals a clear right temporal onset of 6 to 8 Hz rhythmic activity.

In this paper, we present the clinical, semiological, and electroencephalographic findings of this case, highlighting features that have not been previously reported. Additionally, we review pertinent medical literature regarding musicogenic epilepsy.

**Craig Boss, MD**

Delayed Sleep Phase Syndrome (DSPS) is a circadian rhythm disorder that is frequently undiagnosed in adolescents and young adults. DSPS has also been implicated as a contributing factor in Bipolar Disorder. The following case presents a young adult patient with a history of progressive DSPS with the subsequent diagnosis of Bipolar Disorder and underscores the importance of a sleep history in the evaluation and treatment of affective disorders. In addition, this presentation discusses current research investigating circadian genes and their possible association with DSPS and the diagnosis of Bipolar Disorder.

**A. Boster M.D; S. Gebarski M.D., D. Mikol M.D.**

Does disruption of the blood-brain barrier in pre-eclamptic MS patients predispose to increased disease activity?

While the underlying cause of MS is unknown, an important mechanism of injury is the entry of activated immune cells through an impaired blood-brain barrier (BBB). Clinical studies of pregnant women with MS have shown a protective effect with regard to disease activity, particularly during the latter stages of pregnancy. Studies of pre-eclampsia demonstrate focal dysregulation of cerebral blood flow, commonly involving the posterior circulation, which can lead to BBB disruption. There is no literature regarding MS disease activity during pregnancy in the setting of pre-eclampsia. Here we describe a woman with MS who at 38 weeks gestation was admitted for pre-eclampsia.

**Dea Boster**

"Treatment of African Americans with Epilepsy in the Early Twentieth Century"

Although no form of epilepsy has ever been considered unique to a particular racial group in the United States, evidence from medical literature and institutional records in the late nineteenth and early twentieth centuries indicates that perceived racial differences played a role in the framing of epilepsy's causes and prevalence, the semiology of seizures, and the parameters of the "sane epileptic." The supposedly alarming increase of epilepsy among "colored" African Americans after Emancipation became a significant element in discourse on miscegenation and racial degeneration, and provided fuel for eugenics arguments of the hereditary effects of seizure disorders. Constructs of race and disease also had an impact on treatment options for African American persons with epilepsy, in institutional settings as well as other locations. This study examines the effects of social categories of race on medical as well as popular understandings of epilepsy in the early twentieth century.

**Tiffany Braley, MD**

During routine household chores, a 57 year old healthy man carried a bucket with a small amount of water up a flight of stairs. At the top, he turned to dump the bucket into a sink, felt a brief tingling sensation in his thighs and collapsed to the floor. Unable to move his legs, he remained on the floor and within ten seconds developed severe lower back pain.

He presented to a local emergency room where he was found to have a significant flaccid paraparesis. He was admitted and an MRI demonstrated a hyperintense, intramedullary lesion on T2 weighted imaging from T-10 to the conus medularis which was felt to be consistent with transverse myelitis, infarct or malignancy. During a five day course of IV solumedrol, the patient improved slightly but was still unable to walk or bare his own weight. He was then transferred to the University of Michigan Comprehensive Epilepsy Program in February 2005 for evaluation, describing three semiologies. Her mildest spell is described as an auditory aura of either a distorted radio in the background or piano music with distorted human voices followed by slight confusion. The second type of spell begins in the same manner, then progresses to include a sense of being in another place, an inability to speak, and a more prolonged confusion. The most severe type of spell then progresses to a secondarily generalized convulsion.

In this paper, we present the clinical, semiological, and electroencephalographic findings of this case, highlighting features that have not been previously reported. Additionally, we review pertinent medical literature regarding musicogenic epilepsy.

**Musicogenic Seizures – A Rare Form of Reflex Epilepsy**

**Elias Bazakos and Jonathan Edwards**

Musicogenic seizures are an extremely rare and complex form of reflex epilepsy, with only a few cases reported in the literature. We present the case of a 26 year old right handed female, a piano performance graduate student, who began experiencing spells in October 2001. She presents to the University of Michigan Comprehensive Epilepsy Program in February 2005 for evaluation, describing three semiologies. Her mildest spell is described as an auditory aura of either a distorted radio in the background or piano music with distorted human voices followed by slight confusion. The second type of spell begins in the same manner, then progresses to include a sense of being in another place, an inability to speak, and a more prolonged confusion. The most severe type of spell then progresses to a secondarily generalized convulsion.

She reports that her spells only occur while she either hears or plays piano music. On further questioning, she admits that spells can also occur if she is reading piano sheet music and hearing the melody in [her] head. She hears and plays piano music every day as a part of her graduate studies, and since the onset of her spells, she experiences auras with the piano music of various genres and composers. The spells are specific to the piano, both standard and synthesizer, and do not occur in the absence of piano music. General neurological examination, routine EEG, and Brain MRI with temporal lobe epilepsy protocol are normal. Long term monitoring by video and EEG captured a typical spell with secondary generalization while the patient played a keyboard at her bedside. The musical piece was Bach's Goldberg Variations, a previously identified trigger. The ictal EEG reveals a clear right temporal onset of 6 to 8 Hz rhythmic activity.

In this paper, we present the clinical, semiological, and electroencephalographic findings of this case, highlighting features that have not been previously reported. Additionally, we review pertinent medical literature regarding musicogenic epilepsy.
Hunter Brumblay MD, Mila Blaivas MD, Frank La Marca, MD

A Case of C2 Pseudotumor Mimicking Osteolytic Giant Cell Tumor

Background:
Pseudotumor of the spine and skull base is a rare occurrence, usually associated with chronic inflammatory disease or trauma. We report a case of pseudotumor involving the C2 vertebral body with osteolytic characteristics that mimicked giant cell tumor on biopsy. A 39-year old woman presented with 6 months of gradually worsening neck pain and weakness that ultimately rendered her unable to walk on her own. There was no history of trauma, infection, or inflammatory disease.

Imaging:
Plain films of the cervical spine demonstrated an irregular outline of the C2 vertebral body and dens with anterior expansion of the C2 body and a pathological fracture of C2. MRI of the cervical spine demonstrated patchy low T1 signal with intense post gadolinium enhancement of the C2 body and odontoid process, both of which were irregularly outlined. The soft tissue mass, which completely replaced the C2 body, engulfed the vertebral artery on the right while extending into the right pedicle of C2 and encroached upon the spinal canal, producing a small amount of high T2 signal in the cord at this level. CT demonstrated expansion of the C2 vertebra with replacement of bone by abnormal soft tissue in the body, the base of the dens, and the right pedicle. There was mild loss of vertebral height, with multiple cortical breaks of the C2 body and base of the dens, consistent with pathological fractures.

Treatment/Outcome:
A trans-oral biopsy was suggestive of giant cell tumor. Therefore, an aggressive, staged resection of the C2 mass was carried out including: right far lateral submandibular approach; C2 laminectomy and posterior fusion from occiput to C5 with lateral mass screws; and trans-oral excision of the tip of the dens with placement of a titanium mesh cage from the clivus to C3. Final histopathological diagnosis was pseudotumor of C2. The patient did well post-operatively and after 18 months of follow up, her strength had returned to baseline and she was able to ambulate on her own.

Conclusion
Pseudotumor with osteolytic characteristics is a rare occurrence in the cervical spine, especially in the absence of chronic inflammatory disease or trauma. It should be included in the differential diagnosis when histological biopsy results are not conclusive for tumor. The treatment for these lesions is excision of the mass with decompression of neurological structures when necessary and spinal stabilization. The authors also recommend long term radiological follow-up.

Maureen Ceresney, MD

Elevated esophageal pressures during vagal nerve stimulation in a patient undergoing continuous positive airway pressure titration.

Abstract -- Vagal nerve stimulation (VNS) therapy has been reported to cause elevated esophageal pressures and alterations in respiration during sleep in patients with and without a prior history of obstructive sleep apnea. The author presents a patient with medically refractory epilepsy and obstructive sleep apnea who underwent a continuous positive airway pressure (CPAP) titration and displayed continued elevations in esophageal pressures during VNS firing at settings where esophageal pressures were otherwise in the normal range.

John A Cowan, Jr. MD, William F. Chandler, MD

Changing Trends in the Utilization and Costs of Procedures performed by Neurosurgeons in the United States.

Introduction: Understanding the changes in procedure utilization and total cost associated with the care of patients is important to the practice of neurosurgery. This investigation quantifies the overall trends in discharge rates and hospital charges for procedures commonly performed by neurosurgeons in the United States.

Methods: Clinical data was collected from the Nationwide Inpatient Sample (NIS) for the years 1997 to 2003. Diagnostic Related Groups (DRGs) that pertain to procedures performed by neurosurgeons (DRG 1-8, 214, 215, 484, 496-500, 519, 520, 529-532) were used to generate the weighted sample population (estimated N=6,172,258). Discharges and total hospital charges annually for craniotomy, spinal procedures (with and without fusion), peripheral nerve procedures (PNP), and extracranial vascular procedures (EVP) were assessed. Population adjustments were made based on US census data and dollar values were adjusted using the consumer price index (CPI) for hospital-related services.

Results: Overall hospital discharges increased from 823,972 in 1997 to 937,020 in 2003 (14%) (P<.001). For all spinal procedures discharges increased from 485,302 to 612,606 (26%) (P<.001). Of these, 50,042 (10.3%) in 1997 and 310,749 (50.7%) in 2003 were for spinal procedures. Discharges for craniotomy increased from 142,622 to 163,669 (14%) (P<.001) and from $7.0 to $10.3 billion for craniotomies (P<.001). Peripheral nerve procedures increased by $1 billion (P<0.001) and EVPs decreased by $0.5 billion (P=0.003).

Conclusions: Spinal procedures experienced large increases in overall utilization and charges during this period. There was a dramatic increase in the number of spinal fusions. Smaller increases were found for craniotomy and peripheral nerve procedures. Extracranial vascular procedures experienced a decline in both utilization and charges. The findings here demonstrate the dynamic nature of the contemporary practice of neurosurgery and have implications for future workforce, training, and research needs.

Praveen Dayalu MD
Emetine (the active component of ipecac syrup) can cause a rare reversible myopathy that is seen most often in women with eating disorders. Presented here is a case involving a child. A nine-year old boy developed refractory nausea and vomiting for several weeks followed by cardiomyopathy and proximal muscle weakness, with very high creatine kinase. After an extensive unrevealing workup, he was found to have high levels of emetine, suggesting child abuse. There were corresponding changes seen on muscle biopsy, which are reviewed. His weakness and creatine kinase levels improved upon stopping further ingestion. Conclusion: In the evaluation of myopathy in children, particularly in the setting of nausea with vomiting or cardiomyopathy, consideration should be given to chronic emetine poisoning, as the condition is reversible and can be a clue to underlying child abuse.

Sonia Eden, MD; Michele Heisler, MD; Karin M. Muraszko, MD; Lewis Morgenstern, MD

Racial and Ethnic Disparities in Cerebrovascular diseases: The Importance to the Practicing Neurosurgeon

STUDY DESIGN: Systematic Review

INTRODUCTION:
There is strong evidence for racial/ethnic disparities in surgical procedures in a number of fields. However, the evidence regarding racial/ethnic disparities in neurosurgical procedures remains more ambiguous. The purpose of this article is to summarize the current literature regarding racial/ethnic disparities in the surgical treatment and outcomes of three different cerebrovascular disease entities: carotid stenosis, intracranial aneurysm, and cerebral arteriovenous malformation (AVM).

METHODS:
We performed MEDLINE (OVID), EMBASE, CINAHL, and Science Citation Index (Web of Science) searches of the literature published between January 1,1966 and December 10, 2005. Main outcome measures examined were racial/ethnic differences in procedure utilization rates and peri-operative stroke, death, and complications.

RESULTS:
36 articles pertaining to racial/ethnic differences in procedure utilization and outcomes were identified. These studies provided high-quality evidence for racial/ethnic disparities in carotid endarterectomy and outcomes following this treatment as well as for disparities in outcomes after craniotomy for aneurysm clipping. No studies investigated racial/ethnic differences in surgical treatments and outcomes of patients with AVMs.

CONCLUSIONS:
Although epidemiological and clinical data on racial/ethnic disparities in frequency and outcomes of certain cerebrovascular diseases exists, the results of this comprehensive literature review suggest that several questions remain unanswered and the actual scope of disparities in neurosurgical care warrants further scrutiny. Race-associated differences in neurosurgical outcomes must be documented and vigorously investigated in order to determine the basis of the observed differences and ensure that we are providing the best care possible to all of our patients.

REFERENCES:
Modified Extended Middle Fossa Craniotomy for Hearing Preservation in Acoustic Neuroma Surgery

**Introduction:** Hearing preservation after resection of an acoustic neuroma (AN) using the middle cranial fossa (MCF) approach has ranged from 20% to 86%. Comparing studies is difficult due to multiple methods of hearing assessment. We have incorporated elements of the extended MCF approach to improve exposure and outcomes in AN surgery.

**Methods:** 74 patients who underwent a modified extended MCF approach for AN resection were identified prospectively and analyzed retrospectively. Hearing was categorized using standardized American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS) guidelines. Facial nerve function was assessed using the House-Brackmann scale. A comprehensive review of the literature was performed to compare our results with those from similar studies.

**Results:** Of 34 patients with class A hearing preoperatively, 21 (62%) remained in class A, 6 (18%) deteriorated to class B, and 7 (20%) deteriorated to class D postoperatively. Overall, 27 (80%) of 34 patients presenting with class A hearing maintained class A or B hearing postoperatively. At 4 months, facial nerve function was House-Brackmann grade I in 61 (85%), grade II in 8 (11%), and grade III in 3 (4%).

**Conclusions:** Postoperatively, 80% of patients who had presented with class A hearing remained at or near that level and 96% of patients had House-Brackmann grade I or II facial nerve function. These outcomes match or exceed published results by nearly every method of comparison. The extended MCF approach modification provides a wider working angle which, along with strictly sharp dissection in a medial to lateral direction, decreases cranial nerve traction and injury during tumor manipulation and increases rates of hearing preservation.

Mark Garwood, MD

---

**Pseudo-REM Sleep behavior disorder (RBD): case report**

**Background:** REM Sleep behavior disorder (RBD) is a parasomnia occurring during REM sleep with loss of muscle atonia allowing a patient to act out unpleasant dreams. Previous reports have suggested obstructive sleep apnea (OSA) can induce agitated arousals from REM sleep with dream-related complex, violent behaviors with normal muscle atonia during REM sleep. Some have labeled this phenomenon pseudo-RBD, which has been reported to resolve with CPAP administration by at least one center.

**Objective:** To report a case of RBD, in a patient with OSA with complete resolution of RBD on CPAP therapy. Therefore, enabling further discussion and review of the relationship between OSA and RBD

**Materials/Methods:** Case Report with polysomnographic illustrations.

**Results:** A 61 year-old man presented with a long history of snoring, excessive daytime sleepiness, and gasping arousals. Over the last 6 years he has had increasingly frequent episodes of acting out dreams that could be frightening and include punching and kicking. Polysomnography showed OSA with an AHI of 53.2 and minimum oxygen saturation of 88%. An episode of isolated increased EMG tone during REM sleep and a period of yelping, moving, and talking during REM sleep was seen. A subsequent titration showed the BiPAP setting of 11/6 cm of water with Bi-flex of 3 to be effective in treating his obstructive sleep apnea. During REM sleep occasional episodes of increased EMG tone were seen with jerking of arms or legs but without complex behaviors. At 3 month follow-up no dream enactment behavior was reported since prior to BiPAP initiation, and excessive daytime sleepiness, snoring, and gasping arousals had resolved.

**Conclusions:** Lack of REM sleep muscle atonia in our case of complex aggressive behavior associated with OSA suggests both RBD and pseudo-RBD may be seen in patients with OSA. Arousalus are known to precipitate parasomnias. Arousals secondary to OSA may lower the threshold necessary in a patient predisposed for RBD, allowing RBD to occur, as well as lead to pseudo-RBD by causing awakenings from REM sleep with similar symptomatology to RBD but with normal muscle atonia in REM sleep.

Kerry Hulsing

---

**Employment in Refractory Epilepsy**

**Purpose:** To investigate employment status and factors associated with unemployment in people with medically refractory epilepsy being treated at the University of Michigan.

**Methods:** Data were collected from 36 adult epilepsy patients undergoing evaluation for surgery for medically refractory epilepsy.

**Results:** The unemployment rate in this population was 72%. Employment status did not correlate with availability of transportation, number of seizures per week, or perceived level of family support. Those that were employed had attained a higher level of education on average, with 40% having a Masters level or higher degree, compared to 11% in the unemployed population. Depression and anxiety were reported more frequently and a lower quality of life was described in the unemployed population. Seizure control was ranked as the primary reason hindering employment by 96% of the unemployed. The importance of employment to quality of life was rated very highly by both the employed and unemployed.

**Conclusions:** Employment status is a significant issue for people with medically refractory epilepsy. While absolute number of seizures did not correlate with employment status, lack of seizure control was thought to be the primary problem preventing employment by the majority of respondents. The impact of employment on quality of life also suggests that this issue needs to be continually addressed in this patient population.

---

**Causes of Mortality on a University Hospital Neurology Service**

**Quality assurance case discussions of all patients (n=6012) admitted to a neurology service from 1996 to 2003 were reviewed to determine frequency and causes of mortality. All cases of mortality were reviewed in detail.** The majority of patients (98%) survived their admission; 118 patients died. In 95/118 cases, care had been withdrawn at the time of death. In 11 cases, adverse events occurred during the patient's hospital stay, and may have impacted outcome. Few patients (18%) had clear advance directives. Most mortality in this acute care neurology setting occurs in the course of stroke, epilepsy or complicated tumor management, and is managed through withdrawal of care with family participation.
David Kuhlmann, MD, Todd Arnedt, Ph.D., Flavia Consens, MD

Sleepiness, Fatigue, Mood and Vigilance in Rotating and Non-Rotating Night-shift Medical Workers

Objectives: To compare mental alertness before and after a night shift between nurses who work strictly night shifts and nurses who rotate between day and night shifts.

Methods: For five days prior to a predetermined night shift, five subjects (two straight night shift and three rotating night shift nurses) wore an actigraph watch to measure their daily activity level. This was compared to a sleep log that was filled out concurrently to determine the subject’s sleeping schedule. The nurses were then given tests before and after a night shift to measure their levels of fatigue, vigilance and cognitive performance.

Results: There were no statistically significant differences in performance in any of the three neuropsychological tests between the rotating and non-rotating night shift nurses before or after the night shift studied.

Discussion: While the tests used in the experiment to measure fatigue, vigilance, and cognitive performance did not demonstrate any significant differences, the study was limited by a small sample size, which may have negatively skewed the results. Furthermore, tests that measure sleepiness and mood were not included in the survey. Tests that assess these parameters might have demonstrated significant changes, and could be included in future research.

Raj Kumar, MD

Transcranial electrical stimulation (Tc) motor evoked potential (MEP) is a new evolving intraoperative neurophysiological monitoring technique used at University of Michigan Medical Center Ann Arbor for more than a year. This technique assesses the integrity of motor pathways in the brain as well as spinal cord and is widely used in brain tumour as well as almost all spinal surgeries. Subcutaneous scalp corkscrewed electrodes are placed and electrical stimuli (1 millisecond in trains of five) are applied within a predetermined range of voltage (100-750 volts). Recording is done with subdermal electrodes placed at lower abdominals, Adductor longus, vastus lateralis, tibialis anterior, abductor hallucis brevis, Triceps, Biceps, Abductor Pollicis Brevis muscles bilaterally.

We will be presenting retrospective study involving all patients who have undergone TcMEPs at our center and evaluate the complications arising from this procedure. We will be looking for any seizures either in the OR, immediately after surgery or later on up to 2-3 months of follow up. We will review the incidence of intraoperative oral trauma (tongue or lip bite, dental injury), cardiac arrhythmia, minor scalp burns arising during this procedure. Data will be gathered through review of the medical charts. In the event that a significant number of complications are discovered, we will review a historical control group of charts from patients who have undergone SSEP monitoring without MEPs for similar surgical procedure.

Daniel K. Leventhal and Dominique M. Durand

LONG-TERM EVALUATION OF A NERVE RESHAPING ELECTRODE FOR SELECTIVE STIMULATION OF PERIPHERAL NERVES

Peripheral nerve electrodes show promise as interfaces with the nervous system for neuroprosthetic applications. The Flat Interface Nerve Electrode (FINE) is a cuff electrode designed to reshape nerves into favorable geometries for selective stimulation. By elongating nerves in cross section, the area of the nerve – electrode interface is increased, and central fibers are moved closer to the neural surface. Previous work has shown that individual fascicles, and even portions of fascicles, of the cat sciatic nerve can be selectively activated with the FINE, and that nerve reshaping can be accomplished safely. The objectives of this study were to characterize the long-term stimulation properties of the FINE, assess the degree to which nerve reshaping affects stimulation selectivity, and evaluate the safety of the FINE. 12 adult cats were implanted with 3 different FINE designs that reshaped the sciatic nerve to different degrees. Selectivity measurements were made with these electrodes every 2 weeks for at least 3 months. The recruitment properties of the electrodes were stable over time, and the moderately reshaping electrodes were more selective than the other designs. The nerves were harvested, and examined histologically to determine 1) the extent of nerve reshaping, and 2) if there was histological evidence of nerve injury. The geometries of the nerves implanted with wide and medium cuffs were very similar to each other, casting doubt on whether the superior performance of the medium electrodes in the stimulation experiments was due to greater nerve reshaping. Only nerves implanted with narrow cuffs showed evidence of nerve injury. These results suggest that the FINE is a safe, selective interface for neuromuscular stimulation, but that further work is required to optimize its performance.
INTRODUCTION:
Within the field of spinal cord injury and repair, there has been a growing interest in the use of biodegradable scaffolds as an aid to axonal regrowth (1,2). Such scaffolds have been designed with an internal architecture to influence axonal guidance. We present here the novel use of poly-caprolactone (PCL) in the creation and implantation of such scaffolds in a rat spinal cord injury model. PCL is a polyester that hydrolytically degrades over a period of months to one year dependent on structure and molecular weight. Its chemical and mechanical characteristics are well-suited to a spinal cord injury model, but it has not been well investigated in this environment.

METHODS:
Spinal cord implants were designed in a three-dimensional modeling program. Molds for these designs were built utilizing a 3-D wax printer. PCL was cast into the molds through a combined solvent-casting/salt-leaching method. Various molds with differing micro- and macrofeatures were created. These scaffolds were implanted into a region of spinal cord injury via a complete transection model, in which a laminectomy was performed at T8 followed by a transection of the cord at this level and implantation of the scaffold.

RESULTS:
Utilizing this process, we were able to design different architectures, including a 2.8mm diameter scaffold that contained not only 0.5 mm internal guidance channels, but also longitudinally-oriented 50-micron microgrooves. The walls of these scaffolds were made porous via salt leaching using 200-micron sized salt crystals (see figure). These scaffolds were successfully implanted into rats.

CONCLUSIONS:
Using PCL, one can create designed scaffolds which have a specific internal architecture. This process is straightforward and repeatable, yielding a sturdy yet flexible scaffold suitable for implantation. Its characteristics are appropriate from a surgical standpoint as well, including ease of implantation and the ability to suture such a scaffold into place.

REFERENCES:
Rocio Lopez-Diego, MD

Multiple sclerosis (MS) is a debilitating chronic autoimmune disease of the central nervous system. It is thought that initial stages relate to biased activation of pathogenic pro-inflammatory (Th1) responses. MS is initially characterized by a relapsing-remitting course, followed by a progressive phase with more prominent axonal degeneration and neuronal loss. The mechanisms underlying this switch are not completely understood. It is becoming increasingly clear that dendritic cells (DCs) are professional antigen presenters that not only orchestrate the onset of natural immunity, but also play a central role in adaptive responses via modulation of regulatory T-cells (Treg), while there is an important functional feedback between both cell populations. Abnormal dendritic cells have been found in MS patients and their immunophenotype changes as disease progresses. Our hypothesis is that different MS stages are the result of temporal dysregulation of dendritic and Treg cell populations during progression of the disease. This proposal is intended to provide a functional explanation behind how pathological immune changes at different disease stages influence the differentiation and/or expansion of pro-inflammatory T cells in MS patients. We have previously shown that ex vivo DCs from healthy subjects uniformly express surface TGF-beta, which is rapidly lost with DC activation, this expression is functionally significant, leading to inhibition of T cell activation. We will use multiparameter flow cytometry to characterize surface TGF-beta directly on ex vivo DCs in healthy subjects and MS patients at different stages of disease, and will evaluate the functional significance of these observations on CD4+ T cell activation, differentiation, and the generation of T regulatory cells. The extent to which different immunomodulatory therapies influence TGF-beta expression on DCs in MS patients, and the functional consequences, will also be examined.

Jennifer Majersik, MD

Obstructive Sleep Apnea as an Independent Risk Factor for Stroke

The understanding of the relationship between obstructive sleep apnea (OSA) and stroke continues to deepen. OSA is highly prevalent in patients with ischemic stroke both in the acute phase and following neurologic recovery, with research suggesting that it predated the stroke. Untreated sleep apnea promotes established risk factors for stroke such as hypertension and diabetes. Evidence is accumulating that apart from this effect on other stroke risk factors OSA is itself an independent risk factor for stroke. This suggests that screening for OSA and treatment of OSA be more aggressive in patients with and without stroke, although clinical trials are needed to prove that the treatment of OSA will decrease this risk of stroke.

Robert T. Grotta, MD

Literature Review

Advisors: Devin Brown, Flavia Consens

Paul Motika, MD

High grade angiosarcoma of the aortic arch in a patient presenting with multiple embolic strokes

Abstract: Primary angiosarcoma of the aorta is uncommon and its clinical sequels may be quite varied. It is rare for this lesion to initially present with focal neurologic deficits. We describe the case of a 50-year-old woman with multiple neurologic deficits associated with cortical and subcortical ischemic and hemorrhagic lesions, subsequently diagnosed with high-grade angiosarcoma of the aortic arch. We also conduct a brief literature review.
Background: Improvements in the treatment of brain tumors have produced little impact on outcomes over the past three decades. Still, survival for both pediatric and adult brain tumors is known to be maximized by radiographically complete surgical resection. Unfortunately, even with the best microsurgical technique, resection may leave behind residual, MRI-demonstrable tumor. Previous methods designed to delineate residual tumor at the time of surgery have not been effective. We propose a novel method for delineation of neoplastic tissue using dye-loaded multifunctional tumor targeted nanoplatforms (TNP), previously developed in our laboratories.

Hypothesis: TNP will enable gross, visible delineation of brain tumor boundaries during resection.

Objective/Specific Aims: The overall aim of the study is to demonstrate that dye-loaded TNP, targeted with tumor-homing F3 peptide, are capable of delineating experimental gliomas in rats. The following specific aims will be completed to characterize and test targeted, dye loaded TNP:
1. Demonstration of in vitro targeting and optical staining by TNP in MDA-MB-435 cells
2. Demonstration of in vivo tumor delineation by TNP in the rat cranial window model
3. Demonstration of accurate, MRI-confirmed, ex vivo tumor volume estimation of experimental gliomas by TNP staining

Study design: The study design has three phases- each phase addresses an individual specific aim, as listed above. In the first phase of the study, we will qualitatively and quantitatively judge the ability of TNP to stain cells grown in culture that are known to express nucleolin, the ligand of F3. Both F3-expressing and control cells will be cultured and exposed to TNP. They will be observed for visible color change. The concentration of unbound TNP in culture media from F3-expressing cells and control cells will be measured spectrophotometrically. In the second phase of the study, the rat cranial window model will be employed to directly visualize in vivo tumor color change after TNP administration. The dose and duration of TNP administration necessary to induce optimal color change within implanted gliomas will be determined. In the third phase of the study, tumor volume estimates generated by MRI will be compared to tumor volume estimates generated by TNP staining. Tumor volume estimates will first be generated using MATLAB software from MRI scans. Subsequently, animals will receive TNP and gross coronal sections will be created. TNP stained areas of the gross coronal sections will be analyzed with Image-J software to generate tumor volumes. MRI-based tumor volumes will be compared to TNP-based tumor volumes using a t-test.

Results: Only preliminary studies on proposed research have been completed. TNP has been shown to enter cells and cause fluorescence in vitro labeling. TNP loaded with iron-oxide particles has also been shown to cause contrast enhancement of implanted BL gliosarcomas.

Conclusions: Although a great deal of in vitro and in vivo work remains, preliminary data suggests that synthesis of a dye-loaded nanoparticle for intraoperative brain tumor delineation is feasible.

Jared K. Rustad, M.D., Linda Selwa, M.D.

Unihemispheric meningoencephalitis in 37-year-old woman

This is a report of a 37-year-old woman with transient, diffuse unilateral meningoencephalitis. MRI clearly demonstrates involvement of all vascular distributions in the right hemisphere with no inflammation in the left hemisphere. She presented with progressive headache, hemiparesis, hemineglect and homonymous hemianopsia. Investigation for etiology, including CSF viral (HSV, VZV, EBV, CMV) PCRs and cultures, arbovirus panel, AFB and fungal studies, borrelia antibodies, cytology for malignancy, CRAg, and other CSF studies were negative. MRA of head and neck was also unremarkable. The patient had resolution of clinical signs over 3 months, and resolution of imaging findings with serial MRI scans over 9 months without treatment. This case remains cryptogenic, but raises many interesting questions. Very few disease processes in the adult cause diffuse yet transient hemispheric brain inflammation with sparing of the contralateral hemisphere, without regard for vascular distribution. Rasmussen encephalitis is typically unihemispheric, but tends to be progressive and protracted, associated with seizures, and much more common in childhood. HSV encephalitis can cause focal encephalitis, but predominantly affects temporal lobes and has not been reported to involve most of a single hemisphere. Venous sinus thromboses that cause diffuse hemispheric changes classically have bilateral involvement. Other infectious or inflammatory conditions (PML, viral encephalitides, SSPE , MS, ADEM) do not typically cause diffuse unihemispheric inflammation with sparing of the contralateral hemisphere. We feel this case raises important questions about the mechanism of inflammation at the blood brain barrier.

Erica Schuyler, MD

Headache, Hemiplegia and Seizures in a 28 year old woman

Advisor: Nan Barbas

Hemiplegic migraine is a rare condition in which migraine headache is associated with a reversible episode of focal motor weakness. In this poster, I will discuss an interesting case of a 28 year old woman with recurrent hemiplegic migraine and seizures. Clinical details as well as MRI, PET, and EEG studies will be presented. Much of what is known about the genetics of migraine has to do with the study of families with Familial Hemiplegic Migraine, an autosomal dominant condition. In some of these families, this disorder has been linked to specific mutations in ion channels. In the discussion, I will describe the current knowledge of the genetics and pathophysiology of hemiplegic migraine. I will also review the role of genetics in other types of migraine and discuss how the study of the genetics of hemiplegic migraine may help in the understanding of more common types of migraine.
Mihaela Teodorescu, MD

What Predicts Sleep Duration in Patients with Asthma?

Authors: CM Senger, FB Consens, WF Bria, MC Teodorescu, Y Ye, JD Kalbfleisch, J Palmisano, ADurance, RD Chervin, M Teodorescu. University of Michigan, Ann Arbor, MI

Introduction: Asthmatics report reduced sleep quality and excessive daytime sleepiness. We assessed potential contributors to sleep duration in patients with asthma.

Methods: Patients returning for routine follow-up at a tertiary Asthma Clinic completed the Epworth Sleepiness Scale (ESS) and question-items about 24-hour average sleep duration, perceived daytime sleepiness, and asthma symptom frequency (National Asthma Education and Prevention Program guidelines). Medical records were reviewed to help determine asthma severity (step 1 to 4) and search for established comorbid diagnoses such as psychopathology (depression, anxiety, bipolar disorder, and panic disorder) and current medications.

Results: Among 87 subjects, who were not on treatment for sleep-disordered breathing and did not have other lung conditions, age (mean ± sd.) was 45±13 yrs; 66 (76%) were women; body mass index (BMI) was 31±8.5; forced expiratory volume in one second as percent of predicted value (FEV1) was 85.09±21.41; 21 subjects (24%) were in asthma severity step 1, 6 (7%) in step 2, 31 (36%) in step 3, and 29 (33%) in step 4. The mean self-reported sleep duration was 7.05±1.74 hours (range 3.5-12). Twenty (23%) subjects had an established diagnosis of depression and 4 (4.6%) of other psychiatric conditions. Sleep duration correlated only with coexistent psychopathology (Spearman \( \rho =0.233 \), \( p=0.03 \)) and trended toward associations with the use of inhaled corticosteroids (\( \rho =-0.199 \), \( p=0.06 \)) and psychoactive medications (\( \rho =0.194 \), \( p=0.07 \)). No correlations were observed between sleep duration and asthma severity step (\( \rho =0.148 \), \( p=0.17 \)), FEV1%, ESS score, perceived daytime sleepiness, age, gender, BMI, history of allergic rhinitis, gastro-esophageal reflux, inhaled long-acting bronchodilator use, anticholinergic use, or theophylline use. Among the psychiatric diagnoses, only a diagnosis of depression correlated with sleep duration (\( \rho =0.266 \), \( p=0.01 \)). In a final regression model which included depression, inhaled steroid use, and psychoactive medication use as covariates, only comorbid depression was independently associated with sleep duration (general linear model, \( R^2 =0.121 \), \( p=0.05 \)).

Conclusions: In this sample of asthmatics, longer sleep duration was predicted by coexistent psychopathology, in particular depression. Severity of asthma showed no clear correlation with shorter sleep duration. Asthmatics who complain about sleep-related problems should be screened for comorbid psychiatric conditions.
Sheila C. Tsai, Jessica Naff, Mark Opp, and Flavia B. Consens

Mallampati classification and BMI as predictors of severity of obstructive sleep apnea as measured by the apnea-hypopnea index.

Background
Sleep apnea is conservatively estimated to occur in 4% of men and 2% of women aged 30-60 years old, with increasing incidence with advancing age. Some small studies have demonstrated an association between the Mallampati score (MS) used by anesthesiologists to predict the potential difficulty in intubating a patient and the diagnosis of obstructive sleep apnea (OSA). Also, a body-mass index (BMI) greater than 30 has been associated with the diagnosis of OSA. We recently reported similar findings utilizing our databases.(1) The apnea-hypopnea index (AHI) determined on polysomnogram (PSG) objectively determines the presence of and provides a means of grading the severity of OSA.

Hypothesis
We hypothesize that the Mallampati score in conjunction with body mass index (BMI) may help predict the severity of an individual¿s OSA as measured by the AHI.

Methods
The University of Michigan Sleep Laboratory has a database of 17,005 consecutive PSGs performed between 3/4/85 – 4/23/03. This data set contains a number of parameters including AHI. The University of Michigan Department of Anesthesia also manages a database of 17,386 consecutive surgical cases performed at the University Hospital from 6/1/04 - 8/9/05, which also contains parameters including MS and BMI. When multiple PSGs were noted for the same patient, the AHI from the earliest dated study was used, under the assumption that this was the patient¿s baseline PSG. When more than one surgery was performed, the data from the earliest surgical date was used. The merged data was then analyzed for a correlation between the AHI and the MS and BMI at the time of surgery.

Results
A total of 209 patients had both polysomnographic and peri-operative information during the specified time periods. This group included 108 males and 101 females, with an age ranging between 17 – 85 years old. The mean ± SD for our parameters of interest were as follows: AHI = 23.8 ± 27.2, minimum oxygen saturation (mO2) recorded on the PSG = 82.2 ± 12.1%, BMI = 32.8 ± 8.9. MS were divided into 2 groups: I&II and III&IV, with 85.4% of patients within the former group and 14.6% within the latter group. AHI was divided into 2 groups: < 30 and ≥30, with 74.2% in the former and 25.8% in the latter group. The correlation between the AHI and BMI was 0.127 (p=0.069). The correlation between the dichotomized AHI and MS variables was 0.004 (p=0.952).

Conclusions
In addition to a patient¿s clinical history, previous reports have indicated that relatively simple physical examination findings, as MS and BMI, may be used to help predict the presence of OSA. The current finding suggests that these findings may not help as predictors of severity of OSA as defined by AHI. We postulate that physical findings may behave similarly to subjective symptoms, as excessive daytime sleepiness, where there is no clear correlation between their presence and severity of OSA as defined by AHI. Although further analysis is required to fully interpret the significance of our data, the merged databases from the University of Michigan Sleep Laboratory and the Department of Anesthesiology may provide a wealth of information into the pathophysiology and peri-operative findings in patients with OSA.

Reference:

Kara Warden, MD

<table>
<thead>
<tr>
<th>Title:</th>
<th>Ocular Myasthenia Gravis with Multiple Episodes of Spontaneously Remitting Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Introducti on:</td>
<td>Myasthenia gravis is a chronic disease generally requiring lifelong treatment. Approximately 20% of patients with myasthenia gravis will have a spontaneous transitory or complete clinical remission during the course of their disease. Although a relapsing remitting course is common in patients on immune modulating treatment, there are only a handful of published cases describing patients with multiple episodes of spontaneously remitting ocular myasthenia gravis.</td>
</tr>
<tr>
<td>Metho ds:</td>
<td>A retrospective case series of seven patients with oculocutaneous myasthenia gravis confirmed by AChR Ab, or electrodiagnostic testing.</td>
</tr>
<tr>
<td>Resu lts:</td>
<td>The number of years from onset of symptoms to the time of diagnosis ranged from 1 – 15 years. During this period, the number of recurrent episodes ranged from 2 to 12 with each lasting 2 – 10 weeks. No precipitating factors were identified and each remission occurred spontaneously. Symptoms generally consisted of diplopia and/or ptosis.</td>
</tr>
<tr>
<td>Conc lusio n:</td>
<td>This unusual presentation of MG should be in the differential diagnosis of patients with single or multiple cranial neuropathies that spontaneously resolve or in patients with multiple episodes of spontaneously resolving cranial neuropathies. Testing for MG is relatively inexpensive and non-invasive and may prevent an expensive and unnecessary work-up and lead to appropriate therapy.</td>
</tr>
</tbody>
</table>
Jackie Whitesell, MD

Case report of CADASIL in patient with family history of early onset stroke.

We present here a 43 year-old man transferred from an outside hospital with sudden onset of left sided face, arm, and leg weakness as well as dysarthria and difficulty walking. The majority of his symptoms improved within fifteen minutes. During his hospital course his dysarthria and left sided hemiparesis also improved. He denied any headache associated with these symptoms. He did have a history of occasional mild headache, but denied severe or frequent headaches. Lumbar puncture at an outside hospital was unremarkable. MRI of the brain showed numerous confluent subcortical, deep, and periventricular white matter abnormalities with high T2 and Flair signals. There was restricted diffusion in the right internal capsule and subcortical white matter as well as the left parietal lobe. There were also at least 10 cystic lacunes in the bilateral frontal and parietal lobes as well as the basal ganglia. MRA of the head and neck was unremarkable. Conventional cerebral angiogram showed normal neck and cerebral vasculature. TEE showed a small PFO with significant right to left shunt. No thrombus was seen. Further family history was obtained including history of stroke and dementia in multiple family members at a young age. This raised the suspicion for Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL). Dermatology was consulted for axillary skin biopsy. Skin biopsy showed typical granular electron-dense material within multiple vessel walls which was consistent with a diagnosis of CADASIL.

Sources:
Diagnostic Imaging Brain, Osborn, June 2005
Adams and Victor’s Principles of Neurology, Seventh edition, Victor, Maurice and Ropper, Allan; 2001
Careweb notes from 11/30/05, 12/14/05, 3/01/06


Differences in Intracerebral Hemorrhage between Mexican Americans and non-Hispanic Whites

**Background**: Hispanic Americans are the largest minority population in the United States, with Mexican Americans (MAs) comprising the largest subgroup. MAs have higher incidence rates of intracerebral hemorrhage (ICH) than non-Hispanic Whites (NHWs). We present clinical and imaging characteristics of ICH in MAs and NHWs in a population-based study.

**Methods**: This work is part of the Brain Attack Surveillance in Corpus Christi (BASIC) project. Cases of non-traumatic ICH were identified from 2000-2003, and all initial head CT scans were reviewed by study physicians. Multivariable logistic regression was used to assess the independent associations between ethnicity and ICH location (lobar vs. non-lobar) and volume (≥30 vs. < 30 cc), adjusting for demographics and baseline clinical characteristics. Logistic regression was also used to determine the association between ethnicity and in-hospital mortality, adjusting for confounders.

**Results**: A total of 149 MAs and 111 NHWs with ICH were identified. MAs were younger (70 vs. 77, p<0.001), more often male (55% vs. 42%, p=0.04), had a lower prevalence of atrial fibrillation (2.0% vs. 13%, p<0.001), and a higher prevalence of diabetes (39% vs. 19%, p<0.001), with no ethnic differences in the prevalence of hypertension or smoking. MA ethnicity was independently associated with non-lobar hemorrhage (OR 2.08, 95% CI: 1.15, 3.70). MAs had over two-times the odds of having small (<30cc) hemorrhages compared with NHWs (OR=2.41, 95%CI: 1.31, 4.46). NHWs had higher in-hospital mortality, though this association was no longer significant after adjustment for ICH volume, location, age, and gender.

**Conclusions**: There are significant differences in the characteristics of ICH in MAs and NHWs, with MA patients more likely to have smaller, non-lobar hemorrhages. These differences may be used to examine the underlying pathophysiology of ICH.

Disclosure: This study was funded by NIH RO1 NS38916.