Subclinical seizures are very common in pediatric traumatic brain injury patients in the first several days after injury and occur in about 25% of patients monitored by continuous electroencephalography.

**Background:** Seizures following traumatic brain injury (TBI) can create diagnostic confusion and cause secondary injury by increasing brain metabolism and increasing intracranial pressure (ICP). Continuous electroencephalography (cEEG) can diagnosis subclinical seizures.

**Objective:** To identify a rate of seizures using a cEEG protocol in children with TBI.

**Design:** Prospective case series.

**Methods:** Patients with severe and moderate TBI (Glasgow Coma Scale [GCS] score 3-12) from 2009 to 2013 had cEEG monitoring with video accompaniment for at least 48 hours beginning as soon as possible after admission. Patients were treated with levetiracetam and had serum sodium monitored at least 4 times per day. Brain Trauma Foundation Guidelines were used for management. Seizure rate was the primary outcome. Seizure was defined as paroxysmal EEG discharge that evolved over time and location on cEEG. Subclinical seizure was defined as seizure without corresponding noticeable clinical manifestations. Status epilepticus was defined as continuous seizure activity >30 minutes or multiple seizures constituting >50% of monitoring time.

**Results:** There were 594 patients with TBI and 144 with cEEG; 102 had moderate-to-severe TBI. Mean age was 4.3 years and mean GCS was 7.7. In total, 93% received prophylactic anticonvulsants; 75% received treatment prior to cEEG placement. cEEG monitoring was started within a median of 6 hours after injury. Overall, 43 patients (30%) had seizures on cEEG; 17 had subclinical seizures, 23 had clinical and subclinical seizures, and 3 had only clinical seizures. There were 23 patients with status epilepticus. Seizure onset ranged from 2 minutes to 3 days after monitoring started. The first seizure was with 12 hours of beginning cEEG monitoring in 51% of patients. Abusive head trauma and age were the only predictors of seizures in univariate analysis. Age 2.4 years dichotomized the cohort. Age was the only predictor of seizures in multivariate analysis because abusive head trauma was present in the younger patients. Patients with seizures had longer hospital length of stay, but no relationship to discharge disposition.

**Conclusions:** cEEG identifies a significant number of children with subclinical seizures after TBI. Risk of seizures is highest in those with age <2.4 years.

**Reviewer’s Comments:** This study shows that subclinical seizures are very common in pediatric traumatic brain injury patients in the first several days after injury and occur in about 25% of patients monitored by cEEG. We should keep these data in mind when we encounter clinical changes or intracranial pressure elevation in patients not being monitored by cEEG. Unfortunately, the study did not address the clinical consequences of the seizures. Nor did the study address intervention of the seizures, which is important to know because almost all of these patients were on levetiracetam for seizure prophylaxis. Perhaps a different prophylactic antiepileptic agent should be considered. (Reviewer-N. Scott Litofsky, MD, FACS).

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Keywords: Continuous Electroencephalography, Traumatic Brain Injury, Subclinical Seizure

Print Tag: Refer to original journal article
To Rest or Not to Rest With TBI?

*Benefits of Strict Rest After Acute Concussion: A Randomized Controlled Trial.*
Thomas DG, Apps JN, et al:

*Pediatrics* 2015; 135 (February): 213-223

Over the past 10 years, emergency department visits for sports-related traumatic brain injury have jumped 60%.

**Background:** Pediatric head trauma is a significant part of emergency medicine practice. Over the past 10 years, emergency department (ED) visits for sports-related traumatic brain injury (TBI) have jumped 60%. The common practice for those able to be discharged after a concussion is to go home and rest. However, defining "rest" has been a moveable target. Is it 24 to 48 hours? Is it longer? Is it "cocoon therapy" during which the patient spends days in a darkened room? There are no pediatric studies that have tested the efficacy of strict rest after a TBI.

**Objective:** To evaluate whether recommending strict rest would improve concussion recovery and outcome in children having sustained a TBI and who were discharged from an ED.

**Design:** Prospective analysis.

**Participants:** 99 patients enrolled with 88 completions (45 in the study group and 43 controls); patient age range was 11.0 to 22.0 years (median age, 13.7 years).

**Methods:** Patients diagnosed with mild TBI/concussion were recruited within 24 hours after having presented to a pediatric ED. In the ED, they all underwent neurocognitive, balance (double leg, single leg, tandem stance conditions), and symptom assessment. They were then randomized into 2 groups: (1) those who received discharge instructions advising strict rest for 5 days (intervention cohort) and (2) those who received the usual discharge instructions, namely 1 to 2 days of rest followed by a gradual return to activity (control cohort). Parents kept diaries of symptoms (physical, cognitive, emotional, and sleep) and activity levels (mental and physical). At 3 and 10 days post-concussion, subjects underwent further neurocognitive and balance evaluations.

**Results:** Both the study and control groups reported a 20% drop in energy exertion and physical activity levels. Between the second and fifth day post-concussion, school and after-school attendance was different between groups: 3.8 hours total for the intervention group and 6.7 hours total for controls ($P < 0.05$). When neurocognitive and balance testing were assessed on days 3 and 10, results were no different between groups. However, the intervention group's diaries logged more symptoms over 10 days (total symptom score: 187.9 for the intervention group and 131.9 for controls; $P < 0.03$) and a slower resolution of those symptoms.

**Conclusions:** Strict rest after a concussion not only was not beneficial for recovery in the pediatric population but also it may have contributed to increased symptom reporting.

**Reviewer's Comments:** The majority of both groups sustained the following symptoms: dazed or stunned, confusion, answered slowly, or repeated questions. Loss of consciousness occurred in 36%, anterograde amnesia in 27%, retrograde amnesia in 18%, and seizures in 1%. And yet, only 26% had a CT. I wonder what the percentage would be in a general ED. (Reviewer-Paul P. Rega, MD, FACEP).

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Keywords: Mild Traumatic Brain Injury, Concussion

Print Tag: Refer to original journal article
More than 500,000 emergency department visits in the United States are associated with blunt head trauma in kids.

**Background:** More than 500,000 emergency department (ED) visits in the United States are associated with blunt head trauma in kids. While most are benign, there is a cohort that present with persistent histories of headache. Does that type of history discriminate between those with clinically important traumatic brain injury (cTBI) and those without?

**Objective:** To evaluate the clinical importance of isolated headaches in children who have sustained minor, but non-trivial, blunt head trauma.

**Design:** Prospective observational study.

**Participants:** 27,495 eligible patients (12,675 with headaches) aged 2 to 18 years and with Glasgow Coma Scale (GCS) scores between 14 and 15.

**Methods:** Data were collected from 25 centers in the Pediatric Emergency Care Applied Research Network (2004 to 2006). Histories and physical examinations were conducted as usual, with particular emphasis on documenting the nature of the headache post-trauma. Imaging results were documented if ordered. Outcome measures were: (1) cTBI and (2) TBI objectively diagnosed on CT imaging.

**Results:** Of patients with headache and complete data, 2462 (19.6%) had isolated headaches after minor, but non-trivial, blunt head trauma. None of these had cTBI (0%; 95% CI, 0% to 0.1%). Meanwhile, in the non-isolated headache group, 162 of 10,105 controls had cTBI (1.6%; 95% CI, 1.4% to 1.9%). Risk difference was 1.6% (95% CI, 1.3% to 1.9%). TBI on CT imaging was positive in 3 of 456 patients in the isolated headache group (0.7%; 95% CI, 0.1% to 1.9%) compared to 271 of 6089 patients in the non-isolated headache group (4.5%; 95% CI, 3.9% to 5.0%). That’s a risk difference of 3.8% (95% CI, 2.3% to 4.5%).

**Conclusions:** For children who have sustained an isolated headache after minor head trauma, risk of cTBI and a positive finding on brain CT are rare.

**Reviewer’s Comments:** This study reinforces the concept of not ordering head CT as a knee-jerk reflex on a kid who comes in with a simple headache after a minor head trauma. Of course, we know mom and dad are there to get the CT in the first place, but armed with this study and the myriad of publications about radiation-induced malignancy in children, the emergency physician should be able to reassure the family that an expert clinical exam is worth more than an x-ray. (Reviewer-Paul P. Rega, MD, FACEP).
Medical Clearance for Patients With Concussion Associated With More ED Visits

Impact of a State Concussion Law on Pediatric Emergency Department Visits.
Mackenzie B, Vivier P, et al:
Pediatr Emerg Care 2015; 31 (January): 25-30

There was an increase in the proportion of emergency department visits for sports-related concussion after the mandated state law for medical clearance for return to play.

Background: There are many states that have initiated a law requiring medical clearance prior to returning to sports for children who have suffered a concussion.

Objective: To evaluate the rates of emergency department (ED) visits before and after a state concussion law was enacted.

Methods: This study took place in Rhode Island where the legislature mandated clearance prior to return to sports after a concussion. The authors reviewed ED visits in patients ages 13 to 17 years from 2004 to 2011. Rhode Island initiated the law in 2010. The authors reviewed visits prior to and after passage of the law. The data collected included demographics, sports played, head imaging, and time of year of the injury. As a comparison control, the authors reviewed ankle sprains during the same period.

Results: There were 59,000 ED visits in this age group. Of patients, 661 were diagnosed with concussion symptoms and 348 had ankle injuries. The majority of sports-related concussions was in males (74%), non-Hispanic whites (82%), and in those with higher socioeconomic status (66%). One-third arrived with emergency medical services and 3% were admitted. There was an overall increase in ED visits in 2008 prior to passage of the law. From 2009 to 2010, there was an increase in fall season sports-related concussion visits prior to the law being passed and after the law was passed. When looking at the proportion of sports-related concussions, the number of ED visits doubled after passage of the law during the fall sports season as compared to the proportion of concussions from 2007 to 2009. There were no differences in ankle injuries seen during the study, except in 2009. The number of head CT scans ordered did not change significantly from year to year.

Conclusions: There was an increase in the proportion of ED visits for sports-related concussion after the mandated state law for medical clearance for return to play.

Reviewer’s Comments: The evidence showed the law had an effect on increasing the vigilance of evaluating concussions in teenagers. The good news is that the increased visits to the ED did not increase the number of head CT scans (radiation exposure to the brain). One may infer that physicians at this ED were feeling more comfortable in diagnosing concussions on clinical findings. If state concussion mandate laws help prevent chronic head injuries, other legislatures should consider laws to help protect young athletes. This will help spare coaches/trainers the burden of sending athletes back to the field too soon after a head injury. (Reviewer-Charles I. Schwartz, MD).

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Keywords: Concussion, State Law, Pediatric Emergency Department, Sports

Print Tag: Refer to original journal article
Notch Signaling Pathway Potential Drug Target in Pediatric Astrocytoma

Notch Signaling Activation in Pediatric Low-Grade Astrocytoma.
Brandt WD, Schreck KC, et al:
J Neuropathol Exp Neurol 2015; 74 (February): 121-131

The Notch signaling pathway plays a role in pediatric low-grade astrocytoma development and may represent a promising drug target.

**Background:** Pediatric low-grade astrocytomas represent the most common primary pediatric brain tumors in children. Since most of these tumors grow slowly and are often well circumscribed, they are especially amenable to surgical resection. A subset of tumors, however, progresses in a more aggressive fashion or are surgically unresectable. Thus, understanding more about their underlying tumor biology may allow for the development of targeted drug therapy.

**Objective:** To test the hypothesis that the Notch signaling pathway plays a role in pediatric low-grade astrocytoma development, and to suggest whether this pathway might be a therapeutic target.

**Methods:** Primary tumor samples from cases of pilocytic astrocytoma (n=18) and other pediatric low-grade astrocytomas (n=4) were collected as well as pilocytic astrocytoma-derived and diffuse astrocytoma-derived cell lines. Immunohistochemistry using antibodies against a downstream activation target of Notch, called HES1, real-time polymerase chain reaction, and gene expression microarray studies were all employed to study the Notch pathway. Pharmacologic inhibition of the tumor cell lines with a γ-secretase inhibitor was also performed.

**Results:** The authors found frequent activation of the Notch signaling pathway reflected by overexpression of various Notch pathway members at the mRNA (*NOTCH1*, *NOTCH2*, *HEY1*, *HEY2*) and protein (HES1) levels in pilocytic astrocytomas at various anatomic sites compared with non-neoplastic brain samples. These changes were not associated with specific *BRAF* alterations. Inhibiting the Notch pathway using a γ-secretase inhibitor resulted in variable, but significant, reduction in cell growth and migration.

**Conclusions:** Notch appears to play a role in pediatric low-grade astrocytoma development, and various Notch pathway inhibitors appear to offer potentially promising new drug targets in these tumors.

**Reviewer’s Comments:** Although the sample size is small, the breadth of assays used to interrogate the Notch signaling pathway – from the protein to the mRNA level – is quite extensive. The reader should be reminded that unlike some other solid tumors, it is very difficult to develop pediatric low-grade astrocytoma cell lines. (Reviewer-T. David Bourne, MD).

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Keywords: Notch Signaling, Pediatric Astrocytoma

Print Tag: Refer to original journal article
PET With Radiolabeled Amino Acid Analog Effective in Pediatric Brain Tumor Detection

The Usefulness of Dynamic O-(2-18F-Fluoroethyl)-L-Tyrosine PET in the Clinical Evaluation of Brain Tumors in Children and Adolescents.
Dunkl V, Cleff C, et al:

PET with fluoroethyl-L-tyrosine is effective for diagnosing new brain tumors and identifying progression or recurrence in pediatric patients.

Background: Radiolabeled amino acid analogs have been useful for diagnosing brain tumors using PET. Experience with amino acid analogs is limited in pediatric patients.
Objective: To determine the diagnostic accuracy of 18F-fluoroethyl-L-tyrosine (FET) in children and adolescents with brain tumors.
Design/Methods: This Danish study retrospectively included 48 patients aged ≤18 years who were referred for FET PET for newly diagnosed cerebral lesions, possible progression or recurrence of previously treated tumors, or assessment of chemotherapy effect.
Results: Among patients with newly diagnosed cerebral lesions (n=26), the maximum tumor-to-background ratio (TBR) was associated with the highest diagnostic accuracy. The optimal cutoff value was ≥1.7. The area under the receiver operating characteristic curve was 0.80. Sensitivity was 79% and specificity was 71%. Positive predictive value was 88%. For patients with suspected recurrence or progression (n=18), kinetic parameters were associated with the best diagnostic accuracy. More specifically, the change in standardized uptake value (SUV) over time differentiated tumor from non-tumor. A pattern where SUV peaked at around 10 minutes and then plateaued or decreased thereafter was associated with tumor. A pattern where SUV continued to increase for >20 minutes was associated with non-tumor. Use of kinetic parameters was associated with a sensitivity of 75% and a specificity of 90%.
Conclusions: FET PET may be useful for diagnosing tumor in newly detected cerebral lesions in pediatric patients or tumor progression or recurrence in pediatric patients with previously treated brain tumors.
Reviewer’s Comments: This study supports the potential diagnostic value of radiolabeled amino acid imaging in pediatric patients with suspected brain tumor. The use of a fluorinated amino acid analog is helpful because of its longer half-life. C-11–labeled tracers can only be used at centers with cyclotrons and skilled radiochemists, while there is some potential for shipping 18F analogs for use at centers without such resources. (Reviewer-Shayne Squires, MD).

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Keywords: Kinetic Pattern, 18F-FET Uptake, Metabolic Imaging, Contrast-Enhanced MRI, Children, FET PET

Print Tag: Refer to original journal article
In children and adolescents with back pain, the cause was conclusively diagnosed by history, physical examination, and radiographs in 9% and by MRI in another 25%.

**Background:** Back pain in children is more common than parents assume. In most cases, the cause is not serious, although we are always on alert for the exceptions. We need a systematic, cost-effective approach to this problem that takes into account the appropriate role of imaging.

**Objective:** To document the prevalence of serious causes of back pain seen in pediatric orthopedic practices and identify factors predictive of a diagnosis.

**Participants/Methods:** During a 2-year interval, all children and adolescents (age range, >4 to <18 years) presenting with back pain were enrolled in a prospective diagnostic study. Participants with a known diagnosis, such as scoliosis, were excluded. The authors studied 261 children with back pain, representing 9% of their clinic volume. Plain radiographs of the whole spine were ordered on all patients. MRI was ordered if there was constant pain, pain present at night, radicular pain, or an abnormal neurological examination. A complete blood count (CBC) was ordered in patients aged <10 years to check for leukemia.

**Results:** The back pain was conclusively diagnosed by history and radiographs in 9% and by MRI in another 25%. The remaining patients were diagnosed as having nonspecific back pain, were referred for physical therapy, and were provided NSAIDs. Factors that predicted a specific diagnosis included male gender, constant pain, lumbar pain, or an abnormal neurologic examination. Pain severity as rated by visual analog scale was not predictive of a diagnosis. MRI findings were lumbar disc herniation, degenerative disc disease, spondylolysis, cord lipoma or tethering, ovarian cysts, sacroiliitis, perineural cyst, hydronephrosis, and ependymoma. The authors did not consider disc protrusion as a positive finding.

**Conclusions:** Fewer than 50% of patients had identifiable pathology after the workup. The authors advocate for MRI rather than bone scan as the second-level imaging tool since MRI can help distinguish soft tissue, neurologic, and retroperitoneal issues.

**Reviewer’s Comments:** This is a practical study. It is worth reading the authors’ algorithm on page 29. I think the need for MRI is rather small. In fact, the need to obtain plain radiographs on all patients is a topic for further study since it provided a diagnosis in only 9% of study participants. One could question the value of obtaining a CBC, since no cases of leukemia or hematologic process were discovered. I prefer to address this with history questions focusing on malaise, appetite, fatigue, weight loss, and fever. (Reviewer-Paul D. Sponseller, MS, MD, MBA).

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Keywords: Back Pain, Magnetic Resonance Imaging, Radiographs

Print Tag: Refer to original journal article
Utility of DSQ-C Better Quantifies, Qualifies Symptoms in Brain Tumor Patients

The Relationship Between Corticosteroids and Symptoms in Patients With Primary Brain Tumors: Utility of the Dexamethasone Symptom Questionnaire-Chronic.

Armstrong TS, Ying Y, et al:

Neuro Oncol 2015; 17 (August): 1114-1120

The Dexamethasone Symptom Questionnaire-Chronic is a simple means of determining the impact of glucocorticosteroid use on the well being of patients with brain tumors.

Background: Glucocorticosteroids, including dexamethasone, are frequently used to control edema caused by brain tumors acutely and at recurrence. Side effects are well described, but optimal dose has not been well studied. The Dexamethasone Symptom Questionnaire (DSQ) and Chronic version (DSQ-C) use questions (17 for the DSQ-C) with a 4-point scale (1 = not all, 2 = a little bit, 3 = quite a bit, 4 = very much) to quantify symptoms and takes patients 2 to 3 minutes to complete.

Objective: To evaluate the value of the DSQ-C while accumulating data in brain tumor patients.

Design: Single-institution retrospective study.

Methods: Patients aged >18 years with primary or metastatic brain tumors were asked to complete the DSQ-C at an outpatient clinic visit. They also completed a demographic data sheet. A clinician completed an accompanying checklist, which included tumor type, Karnofsky Performance Score (KPS), and glucocorticosteroid drug, dose, and duration. Total steroid dose was defined as product of daily dose and total days of use.

Results: 96 patients (65% male, mean age 53 years) with primary tumors (77%) and metastatic tumors (23%) participated. In total, 71 (74%) patients were treated with glucocorticosteroids (mean dose 4 mg/d, median duration 1 month); 25 patients not treated with steroids served as a control group. Median KPS for the glucocorticosteroid group was 80 compared to 90 for non-steroid patients. The mean DSQ-C score for the entire group was 27, and the score was significantly different between steroid and non-steroid patients. The most common perturbations that steroid patients reported included sleep difficulties, increased appetite, and anger (>35% for each symptom). Increased appetite, weight gain, roundness of face, and difficulty standing were significantly associated with steroid use. Longer duration of steroid use was associated with increased and decreased appetite, difficulty standing, and increased thrush. Total cumulative dose increased odds of increased appetite, hiccups, face roundness, depression, and difficulty standing. The DSQ-C demonstrated feasibility, reliability, and validity for symptoms of emotionality, Cushingoid weight changes, Cushingoid skin changes, sleep disorder, and gastrointestinal changes.

Conclusions: The DSQ-C can be used as a screening tool for side effects of glucocorticosteroids in brain tumor patients.

Reviewer's Comments: Glucocorticosteroids are well known to be associated with significant side effects for patients. This study demonstrates the utility of a quick and easy questionnaire to better quantify and qualify those symptoms in patients. These results can help us prepare our patients for some of the discomforts of dealing with their illness and its treatment. The study did not address changes in the DSQ-C score over time or after the patient discontinued steroids; these issues are also worth investigating. (Reviewer-N. Scott Litofsky, MD, FACS).

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Keywords: Brain Tumor, Corticosteroids, Patient-Reported Outcomes, Symptoms

Print Tag: Refer to original journal article
Risks of Temporal Lobe Necrosis Highly Correlated With Radiation Dose

Dose–Volume Relationships Associated With Temporal Lobe Radiation Necrosis After Skull Base Proton Beam Therapy.

McDonald MW, Linton OR, Calley CS:

Int J Radiat Oncol Biol Phys 2015; 91 (February 1): 261-267

The risks of temporal lobe necrosis are greatly associated with radiation dose, and the risks increase when V60 is >5.5 cm³ or V70 is >1.7 cm³.

Background: Temporal lobe necrosis is a well-described phenomenon and is most common in patients treated for central nervous system tumors, but can also occur in the treatment of nasopharyngeal cancers, particularly if a posterior approach is used. The threshold for temporal lobe necrosis was thought to be 54 Gy using conventional fractionation, and this is probably insufficient to cure many skull base tumors.

Objective: To analyze the dose–volume relationship associated with temporal necrosis.

Design: Retrospective review (2004-2012) from the now-closed Indiana University Health Proton Therapy Center.

Methods: Patients who were treated with curative intent and had not received prior radiation therapy were included. Patients had a minimum follow-up of 6 months, and factors analyzed included gender, age, hypertension, diabetes, smoking, and clival versus non-clival tumors. Temporal lobe necrosis was diagnosed by new MRI findings of T1 enhancement with surrounding T2 edema, with or without accompanying clinical symptoms. The first MRI showing temporal lobe necrosis was fused with the treatment plan. Patients were followed with MRIs every 6 months.

Results: There were 66 patients and 131 temporal lobes included (not sure where the last temporal lobe went). The median follow-up was 31 months and 3-year survival was 85%. The incidence of any temporal lobe necrosis at 3 years was 12.4%. Looking only at patients with clinical symptoms of temporal lobe necrosis, the incidence at 3 years was 5.7%. Radiation necrosis occurred in 16 temporal lobes in 12 patients, with a median time to development of 21 months. None of the clinical factors examined was associated with an increased risk. Dose of radiation mattered. A 15% risk of developing temporal lobe necrosis at 3 years was V40 >16.5 cm³, V50 >9.6 cm³, V60 >5.5 cm³, and V70 >1.7 cm³. There were no cases of temporal lobe necrosis when V70 was <0.1 cm³.

Conclusions: The risks of temporal lobe necrosis are highly correlated with dose, and the risks increase when V60 is >5.5 cm³ or V70 is >1.7 cm³.

Reviewer’s Comments: This is a well-written paper. I am surprised that chemotherapy did not increase the risk, but there is always that blood-brain barrier, and the power of the study is limited. For example, there were 8 patients with diabetes and none developed radiation necrosis (P =0.33). (See images for this review at practicalreviews.com.) (Reviewer-Jonathan J. Beitler, MD, MBA, FACP, FASTRO).

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Keywords: Temporal Lobe Necrosis, Temporal Lobe

Print Tag: Refer to original journal article
What Is the Neuropsychological Outcome After DBS for Parkinson Disease?

Neuropsychological Outcome After Deep Brain Stimulation for Parkinson Disease.

Odekerken VJ, Boel JA, et al:

Neurology 2015; 84 (March 31): 1355-1361

There was no difference in neuropsychological outcome with subthalamic nucleus versus globus pallidus interna deep brain stimulation for Parkinson disease.

**Background:** Deep brain stimulation (DBS) of the subthalamic nucleus (STN) and the globus pallidus interna (GPI) has been shown to be very effective in improving motor symptoms in patients with advanced Parkinson disease. Two randomized controlled trials (RCTs) comparing the efficacy of both targets showed no significant difference in motor symptoms or dyskinesias; however, various studies have reported differences in cognitive outcomes between the 2 targets. In a recent RCT, the Netherlands Subthalamic and Pallidal Stimulation (NSTAPS) trial, the authors found that STN stimulation resulted in a greater motor functional improvement in the off-medications phase, yet they found no difference in cognition, mood, or behavior.

**Objective:** To look at the neuropsychological outcomes of the original NSTAPS trial to assess for predictive parameters on cognitive decline after STN and GPI DBS.

**Methods:** Patients from the original NSTAPS trial were included. All patients had idiopathic Parkinson disease with severe motor symptoms and were randomized to either bilateral GPI or STN DBS. Patients underwent formal neuropsychology evaluations prior to surgery and at 12 months postoperatively. Patients and evaluators were blinded to the therapeutic target. This study presents the outcomes of the neuropsychology tests that were performed during the trial, but were not published.

**Results:** Data from 58 GPI and 56 STN DBS patients were available. Baseline cognitive tests between groups showed no significant difference. At 12 months, there was a difference in both the STN and GPI groups in the Stroop word reading and Stroop color naming tests, the Trail Making Test part B, and the Wechsler Adult Intelligence Scale, with a greater negative change with STN. However, there was no significant difference between groups regarding cognitive decline after DBS. Older age and better baseline semantic fluency were found to be predictive of cognitive decline after DBS.

**Conclusions:** This study, looking at a Class I trial of GPI versus STN DBS in patients with Parkinson disease, found no significant difference in neuropsychological outcomes between targets. Predictive values of cognitive decline for either target included advanced age and high baseline semantic fluency.

**Reviewer’s Comments:** This article clearly addresses an area of concern by clinicians regarding the potential for neurocognitive decline following DBS for Parkinson disease. The study shows no significant difference in cognitive outcome between targets; however, with both targets there was a significant decline in 4 neurocognitive tests, with a trend toward worsening decline in the STN group. It is worth noting that patients in the NSTAPS trial underwent surgery earlier in their disease (in their late 40s) than usual for the overall patient population, and their cognition was therefore relatively high at baseline, with a mean Mattis Dementia Rating Scale score of 138. Thus, the findings may not be applicable to many neurosurgical practices. (Reviewer-Jennifer A. Sweet, MD).

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Keywords: Deep Brain Stimulation, Parkinson Disease, Neuropsychological Outcomes

Print Tag: Refer to original journal article
The Lowdown on NPH

Complications Related to the Type of Hydrocephalus: Normal Pressure Hydrocephalus.

Poca MA, Sahuquillo J:

Complications of CSF Shunting in Hydrocephalus: Prevention, Identification, and Management. 2015; Section 11 (): 159-175

There is no standard protocol for diagnosis of normal pressure hydrocephalus.

**Background:** The prevalence of normal pressure hydrocephalus (NPH) is estimated at 0.2% in patients aged 70 to 79 years and 5.9% in those aged ≥80 years (Jaraj et al, 2014). NPH accounts for 4% of all dementias (Fisher, 1982). **Causes:** Secondary NPH is due to subarachnoid hemorrhage, meningitis, trauma, etc. **Diagnosis:** Clinical Triad: Wobbly gait or gait ataxia is characterized by a slow, shuffling, hesitant, and broad-based gait. Walking is difficult on a slope or stairs. Getting up or sitting is challenging, and patients have impaired attention, concentration, and short-term memory. Fine motor skills are compromised. Urinary incontinence evolves from increased frequency, to urgency, to uncontrolled incontinence; fecal incontinence is rare. Aphasia, agnosia, or paresis as well as progressive dementia without gait disturbance are not suggestive of NPH. **MRI:** Enlarged ventricles are out of proportion with the cortical atrophy. The fourth ventricle can be normal. The Evans Index should be ≥0.3. A better ratio is the ventricular volume/intracranial volume (Toma et al, Neurosurg 2011). The callosal angle is frequently <90 degrees. Often there is a tightness of the high convexity and medial subarachnoid spaces together with a disproportionately enlarged Sylvian fissure. A lumbar tap of 30 to 50 mL is positive if there is improvement of ≥1 point on the NPH scale and on motor tasks such as: rising from a chair, walking 3 m, and coming back and sitting at maximal speed without a walking aid. Improvement can be delayed until the next day and can last 72 hours. An opening pressure >14 cm water is associated with better response to shunting. If the tap is negative, an infusion test is recommended (Kahlon et al, 2002). **Comorbidities:** At a median follow-up of 4.7 years after shunting, almost half of patients have clinical dementia, most likely due to concomitant Alzheimer or vascular dementia (Koivisto et al, Neurosurg 2013). **Treatments:** The sooner, the better. The gold standard is the ventriculoperitoneal shunt with an antisiphon or gravity-compensating device. A lumboperitoneal shunt, a third ventriculostomy, and acetazolamide are all less-accepted therapies.

**Reviewer's Comments:** Complications from shunting range from 5% to 100% and consist of mostly revisions, overdrainage, or malfunction. Life-threatening complications include intracerebral and subdural hematomas as well as infection. Less serious complications include obstruction, hygromas, positional headaches, abdominal pain, transitory hypoacusia, or tinnitus. Obese patients have high intra-abdominal pressure, and antisiphon or gravity-compensating devices might have to be removed. Incorrect valve selection or shunt malfunction should be suspected in patients with positive diagnostic criteria who fail to improve after surgery. Functional improvement is the goal. In total, 29% to 96% benefit from shunting (Poca et al, 2012). (Reviewer-Luc Jasmin, MD, PhD).

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Keywords: Hydrocephalus, Complications, Diagnosis, Treatments

Print Tag: Refer to original journal article
LP Shunt -- A Good First Option for NPH

Kazui H, Miyajima M, et al:

Lancet Neurol 2015; 14 (June): 585-594

At least 60% of normal pressure hydrocephalus patients will benefit from lumboperitoneal shunting.

Background: Idiopathic normal pressure hydrocephalus (NPH) is common and treatable. The recent SINPHONI prospective trial established that 69% of patients had sustained improvement in functional status 1 year after ventriculoperitoneal shunting. Another recent study, this one retrospective, showed a similar percentage of improvement in functional status (64%) 1 year after lumboperitoneal (LP) shunt placement.

Objective: To look at the long-term effect of LP shunt placement on symptoms and signs of NPH.

Design: Prospective, randomized, open-label multicenter trial under the name SINPHONI-2.

Methods: Patients aged 60 to 85 years diagnosed with NPH who fulfilled the selection criteria were randomized to either be immediately implanted with an LP shunt or to wait 3 months and then get implanted. The same programmable valve and an anti-reflux device were implanted in all patients. The valve was adjusted every 1 to 3 months according to clinical evaluation and imaging. The primary end point was an improvement of at least 1 point on the modified Rankin Scale (mRS) at 3 months and 12 months compared to preoperatively. Secondary end points included the idiopathic normal pressure hydrocephalus grading scale, the timed 3-m up-and-go test, the Mini-Mental State Examination, the Frontal Assessment Battery, level of independence in activities of daily living as well as others.

Results: From 2010 to 2012, 49 patients were immediately implanted and implantation was postponed for 3 months in 44. There were more women in the postponed group (68%), but otherwise the 2 groups were comparable in age (76 years) and duration of symptoms (22 to 27 months). The mean time from diagnosis to implantation was 17 days for those immediately treated. At 3 months, 65% of the treated and 5% of the nontreated had an improvement of at least 1 point on the mRS. After 12 months, when all patients had been implanted with an LP shunt, a similar percentage of patients improved at least 1 point on the mRS (67% for those who had the early surgery and 58% for those who had the surgery at 3 months). Two patients had surgical subdural hematoma and 4 had shunt tube migration in the early implanted group compared to 1 with surgical subdural hematoma and 1 with shunt tube migration in the late implanted group.

Conclusions: LP shunt could be a first line of treatment for NPH.

Reviewer’s Comments: The authors cite a technical paper that describes how to reduce the migration of the abdominal portion of the catheter (Kawahara et al, Inn Neurosurg 2013:1;169-172). Maybe one day shunts will be a thing of the past. I would suggest reading the results of a small clinical study by Ivkovic and colleagues (Fluids and Barriers of the CNS, 2015) showing that acetazolamide improved both the clinical and imaging signs in NPH patients. (Reviewer-Luc Jasmin, MD, PhD).

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Keywords: Idiopathic Normal Pressure Hydrocephalus, Lumboperitoneal Shunt, Outcome, Randomized, Prospective

Print Tag: Refer to original journal article
It is critical to consider the effects of age, race, sex, and body mass index as well as their interactions on intracranial measurements in determining the volume of posterior fossa and total intracranial volume in adult patients with Chiari 1 malformation.

**Objective:** To evaluate the effects of demographics on the volume of posterior fossa and total intracranial volume in adult patients with Chiari malformation type 1.

**Design:** Retrospective study of 28 patients with Chiari 1 malformation, 21 patients with idiopathic intracranial hypertension, and 113 control subjects who underwent brain MRI between January 2010 and January 2012.

**Methods:** All patients underwent a total of 12 linear measurements of the intracranial compartment and posterior fossa. Manual segmentation of the posterior fossa volume and total intracranial volume was performed on sequential sagittal contrast-enhanced 3-dimensional gradient-recalled echo T1-weighted images using AW Suite software, and ratios of posterior fossa volume to total intracranial volume were calculated for all patients. Demographic differences among patients with Chiari 1 malformation, patients with idiopathic intracranial hypertension, and control subjects were assessed using multinomial logistic regression, with patient type as outcome using age, race, sex, and body mass index (BMI, weight in kilograms divided by the square of height in meters) as predictors. Comparison between subjects was then performed using both logistic and linear regression models while controlling for age, sex, race, and BMI.

**Results:** 3 of 12 linear measures (intracranial height, intracranial width, and intracranial length) were statistically significant predictors of total intracranial volume in control subjects and accounted for 74% of the variance in total intracranial volume. Four of 12 linear measures (intracranial height, posterior fossa height, posterior fossa width, and posterior fossa length) statistically significantly predicted posterior fossa volume and accounted for 54% of variance. Sex, race, and BMI were statistically significantly associated with posterior fossa volume. The effect of age was not statistically significant. For total intracranial volume, sex, race, and BMI were statistically significantly associated; however, age was also statistically significant. The ratio of posterior fossa volume to total intracranial volume was predicted by age, sex, race, BMI, and the interactions of age with sex, and of race with BMI. No statistically significant differences in posterior fossa volume, total intracranial volume, or ratio of posterior fossa volume to total intracranial volume were seen between the Chiari 1 malformation group and the control group after controlling for demographics. Patients with idiopathic intracranial hypertension were more likely than control subjects to have smaller posterior fossa and larger total intracranial volumes.

**Conclusions:** Demographics play a significant role in the size of posterior cranial fossa. It is critical to consider the effects of age, race, sex, and BMI as well as their interactions on intracranial measurements.

**Reviewer's Comments:** I agree with the authors in that size of posterior cranial fossa is influenced by multiple factors and disease processes and may not be a very strong predictor in diagnosing patients with Chiari 1 malformation. (Reviewer-Sebastian Sadowski, MD).

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Keywords: Chiari 1 Malformation, Posterior Cranial Fossa

Print Tag: Refer to original journal article
A recent study found that in patients with symptomatic lumbar spinal stenosis, outcomes were similar between surgery and structured physical therapy, although many patients treated conservatively eventually chose surgery.

**Background:** Lumbar spinal stenosis is a common cause of low back pain and weakness (typically with neurogenic claudication) and frequently leads to surgery. Although trials comparing surgery to conservative care have favored surgery, most of these studies have not had a specified physical therapy (PT) intervention in the conservative group.

**Objective:** To compare surgical decompression with structured PT in patients with symptomatic lumbar spinal stenosis.

**Participants:** Patients aged >50 years with a documented history of lumbar spinal stenosis (by CT or MRI) and neurogenic claudication were eligible. Exclusion criteria included previous spine surgery, vascular disease, and significant spondylolisthesis.

**Methods:** All participants had previously consented to surgery and were identified by spine surgeons after consent had been obtained. Patients were given information about the study and contacted by the study coordinator. If they met the criteria, they were randomized to either going forward with surgery or participating in a specified PT intervention twice weekly for 6 weeks (which included lumbar flexion exercises, general conditioning, and patient education). Patients were allowed to cross over at any time. Primary outcome was patient-reported physical function at 2 years.

**Results:** Enrollment was a challenge. Most patients did not meet eligibility criteria, and 65% who did declined to participate. This led to discontinuation of the trial before meeting targeted patient numbers. The authors enrolled 169 patients; 87 were allocated to surgery and 82 to PT. Follow-up at 24 months was quite good (87%). Ultimately, 47 of 82 (57%) patients in the PT arm crossed over to surgery in the 2 years (with two-thirds doing so in the first 2 weeks). At 2 years, there was not a statistical difference in physical function; both groups improved to a similar degree. There were 3 main groups: (1) patients assigned to surgery, (2) those who ended up with PT alone, and (3) those initially assigned to PT who ended up with surgery. Analysis did not show significant differences among these groups.

**Conclusions:** In patients with symptomatic lumbar spinal stenosis, outcomes were similar between surgery and structured physical therapy, although many patients treated conservatively eventually chose surgery.

**Reviewer's Comments:** In 2008, the Spine Patients Outcome Research Trial (SPORT) was published in the *New England Journal of Medicine* and reported better outcomes for spinal stenosis patients who underwent surgery compared to those managed conservatively. In the nonsurgical patients, <50% received PT. Therefore, Delitto et al embarked on this study to see if adding structured PT would impact outcomes. Unfortunately, studies like this are complicated by significant crossover rates (SPORT had similar issues) and difficulty with recruitment. However, I do believe this study shows that many patients might be able to successfully avoid spine surgery if they get focused physical therapy. (Reviewer-Mark E. Pasanen, MD, FACP).

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Keywords: Spinal Stenosis, Back Pain, Physical Therapy, Decompression

Print Tag: Refer to original journal article
Is MRI Contrast Material Needed When Evaluating Patients With Syrinx?

MRI of a Syrinx: Is Contrast Material Always Necessary?

Timpone VM, Patel SH:

AJR Am J Roentgenol 2015; 204 (May): 1082-1085

Contrast material may not be necessary in evaluating an associated mass in patients with Chiari 1 malformation.

Objective: To evaluate the accuracy of MRI without contrast in detecting an underlying mass in patients presenting with syrinx.

Design/Methods: This was a retrospective evaluation of 87 patients (49 females, 38 males; age range, 2-77 years; median age, 43 years) who underwent MRI of the spine and met the following criteria: syrinx was present, field of view included the entire syrinx and any associated spinal cord signal intensity abnormality, contrast-enhanced MRI of the entire syrinx was performed, and the syrinx was imaged in both the axial and sagittal planes on both T2-weighted imaging and contrast-enhanced sequences. The presence or absence of a syrinx-associated mass lesion was determined using only sagittal and axial T2-weighted imaging. Imaging features considered positive for a possible syrinx-associated mass on T2-weighted imaging included any one of the following: syrinx nodularity, syrinx septations, or a spinal cord signal intensity abnormality or a mass adjacent to the syrinx. The interpreting radiologists were blinded to all clinical and imaging report information. Subsequently using contrast-enhanced T1-weighted imaging as the reference standard, statistical analysis was performed to determine the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of T2-weighted imaging in detecting a syrinx-associated mass lesion.

Results: Pathologic entities associated with the syringes included: 23 mass lesions, 11 Chiari malformations, and 3 chronic spinal cord contusions; the remaining 50 cases were idiopathic syringes. Using sagittal and axial T2-weighted imaging alone for the evaluation of each syrinx, the readers detected no findings suspicious for a syrinx-associated mass lesion in 55 of 87 cases and detected findings suspicious for an underlying mass lesion in 32 cases. Based on T2-weighted imaging alone, reader sensitivity for an underlying mass lesion was 100% (95% CI, 85%-100%); specificity, 86% (95% CI, 74%-93%); PPV, 72% (95% CI, 53%-86%); and NPV, 100% (95% CI, 93%-100%). Interreader agreement was excellent (κ=0.88). Of the 32 positive cases based on evaluation of T2-weighted imaging, there were 23 true-positive cases and 9 false-positive cases.

Conclusions: Unenhanced MRI that includes sagittal and axial T2-weighted imaging sequences appears to have a high sensitivity and high NPV in the evaluation for a syrinx-associated mass.

Reviewer’s Comments: I believe that more robust studies must be undertaken to confirm the findings of this article before we consider eliminating contrast-enhanced MRI sequences when evaluating for a mass in a patient with syrinx. (Reviewer-Sebastian Sadowski, MD).

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Keywords: Syrinx, Contrast Material

Print Tag: Refer to original journal article
What Are the Radiologic Findings in Patients Presenting With Dysphagia After ACF?

Dysphagia Secondary to Anterior Cervical Fusion: Radiologic Evaluation and Findings in 74 Patients.

Carucci LR, Turner MA, Yeatman CF:

AJR Am J Roentgenol 2015; 204 (April): 768-775

After anterior cervical fusion, dysphagia is more commonly noted in patients after surgery in the mid-cervical spine rather than the lower cervical spine.

**Background:** Anterior cervical fusion (ACF) is an increasingly common procedure for treating several cervical spine pathologies, including degenerative disease, neoplasms, and fractures. Neurologic decompression with discectomy, corpectomy, or both is done and then bony fusion is performed with a bone graft or an interbody device. Since there are rarely serious complications, ACF is considered safe, with low morbidity and mortality. However, some patients can experience dysphagia, odynophagia, and hoarseness; these are underrecognized complications. More common in the early postoperative period, swallowing problems are thought to be temporary and of little consequence.

**Objective:** To evaluate patients who had ACF and subsequently underwent radiologic evaluation for dysphagia in order to determine the frequency, cause, and time course of the development of dysphagia after ACF.

**Design:** Retrospective study.

**Methods:** At a single institution, an 8-year period of records was searched for patients who had ACF (n=1789). Out of this group, patients who underwent radiologic evaluation for dysphagia were selected for a final study cohort of 74 patients (48 men, 26 women; mean age, 53 years). Radiologic studies that included video-modified barium swallow studies and esophagography were retrospectively reviewed for location of cervical fusion, placement of surgical hardware or bone graft, fracture or displacement of surgical hardware or bone graft, structural abnormalities in the pharynx and esophagus, and functional abnormalities, including penetration or aspiration. Displacement of the pharynx or esophagus was graded subjectively by severity. Clinical presentation and time course of dysphagia development were determined by patient chart review.

**Results:** Radiologic evaluation for new-onset dysphagia was performed an average of 120 days after ACF. Level of ACF was C1-C3 in 4 patients, C3-C5 in 41 patients, and C5-T1 in 29 patients. While only 2.2% of patients who underwent surgery in the lower cervical spine needed radiologic evaluation, 9.6% who had ACF in the mid-cervical spine needed evaluation for dysphagia. In total, 91% of patients referred for dysphagia had soft tissue swelling with displacement of the pharynx or esophagus. Surgical hardware or bone graft displacement was seen in 18 patients, esophageal perforation in 3 patients, and retropharyngeal abscess in 3 patients.

**Conclusions:** After ACF, 4.1% of patients presented for radiologic evaluation of dysphagia. Dysphagia is more commonly noted in patients after surgery in the mid-cervical spine rather than the lower cervical spine.

**Reviewer's Comments:** Although there were several limitations to this study, the most notable were its retrospective design and the fact that only patients who were referred for radiologic evaluation of dysphagia were included in the study cohort. In my opinion, dysphagia is important to recognize after ACF since it can greatly impact quality of life. (See image for this review at practicalreviews.com.) (Reviewer-Humaira Chaudhry, MD).

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Keywords: Anterior Spinal Fusion, Anterior Cervical Fusion, Dysphagia

Print Tag: Refer to original journal article
Neurosurgery
Volume 15 Number 8: August 15, 2015
Quiz Code: 33327P

To complete the quiz for credit, log onto www.practicalreviews.com. If you have not previously registered at the site, click on “New Customer Registration” located in the right navigational bar and follow the directions. You will need your account number (located above your name on the Table of Contents) and your mailing zip code. To access the quiz, click on the “Take a Quiz” link located in the right navigational bar. Enter the quiz code and select your answers. Once you click Submit, you will receive immediate notification of your score.

Quiz Questions

1. Continuous electroencephalography identifies a significant number of children with subclinical seizures after traumatic brain injury.
   Circle one: True False

2. Thomas et al found that strict rest after a concussion not only is not beneficial for recovery in the pediatric population but also it may contribute to increased symptom reporting.
   Circle one: True False

3. For children who have sustained an isolated headache after minor head trauma, risk of clinically important traumatic brain injury and a positive finding on brain CT are common.
   Circle one: True False

4. Rhode Island’s state law regarding return to play after a concussion increased emergency department visits, but it did not increase the use of head CT scans.
   Circle one: True False

5. There is no compelling evidence that the Notch signaling pathway plays a role in the development of pediatric low-grade astrocytomas.
   Circle one: True False

6. Semiquantitative PET with fluoroethyl-L-tyrosine is approximately 80% sensitive and 70% specific for detecting tumor in newly diagnosed cerebral lesions in pediatric patients.
   Circle one: True False

7. Plain radiographs, history, physical examination, and MRI will detect a cause in >50% of children and adolescents presenting with back pain.
   Circle one: True False

8. The most common side effects caused by glucocorticosteroids in brain tumor patients include sleep difficulties, increased appetite, and anger.
   Circle one: True False

9. The risks of temporal lobe necrosis are highly correlated with radiation dose, and the risks increase when V60 is >5.5 cm³ or V70 is >1.7 cm³.
   Circle one: True False

10. There is a significant difference in neurocognitive outcome between patients with subthalamic nucleus versus globus pallidus interna deep brain stimulation for Parkinson disease.
    Circle one: True False

11. Aphasia, agnosia, or paresis as well as progressive dementia without gait disturbance and lack of progression of symptoms are suggestive of normal pressure hydrocephalus.
    Circle one: True False

12. The long-term (12 months) outcome of lumboperitoneal shunt for normal pressure hydrocephalus is not as good as the short-term (3 months) outcome.
    Circle one: True False

13. The effect of age is statistically significantly associated with posterior fossa volume.
    Circle one: True False

14. Patients with symptomatic lumbar spinal stenosis have similar outcomes if they choose physical therapy or surgical decompression.
    Circle one: True False

15. Based on T2-weighted imaging alone, reader sensitivity for an underlying mass lesion in patients with syrinx is 100%.
    Circle one: True False

16. Approximately 90% of patients referred for dysphagia have soft tissue swelling with displacement of the pharynx or esophagus.
    Circle one: True False
Neurosurgery
Answers for Volume 15 Number 7: July 30, 2015
Quiz Code: 33285P

1. T  Defecation patterns can be improved in neurosurgical ICU patients with a standardized bowel regimen.

2. F  Among patients with severe trauma and major bleeding, early administration of plasma, platelets, and red blood cells in a 1:1:1 ratio worsens outcome.

3. F  Early administration of exogenous progesterone following traumatic brain injury causes reduction in the excitotoxic cascade, leading to measurable benefits in long-term neurologic recovery.

4. T  Increased time on the scene by emergency medical service providers is associated with decreased mortality for undifferentiated trauma patients.

5. F  In young male hockey players, no relationship was found between cortical thickness and any aspect of brain concussion in a recent study.

6. F  The majority of patients thought to have tumor progression after chemoradiation actually have only pseudoprogression.

7. F  In patients with ischemic stroke with a proximal cerebral arterial occlusion, early thrombectomy, as compared with alteplase alone, failed to improve reperfusion.

8. T  In a study by Singh et al, two-thirds of patients with acute encephalitis had a good outcome at 1 year.

9. F  In a busy referral center's experience, Bell palsy represented 60% of all cases of acute facial hemiplegia.

10. F  In a study of 53 cases with unexplained neurologic decline, autopsy confirmed the diagnosis made at brain biopsy in every case.

11. F  A short course of steroids at the time of multilevel anterior cervical discectomy and fusion does not improve acute dysphagia or airway compromise.

12. T  In a long-term follow-up study by Wood et al, nonoperative treatment of stable thoracolumbar burst fractures was associated with less pain compared to operative treatment.

13. T  In patients with spina bifida who undergo scoliosis correction via spinal fusion, the postoperative Cobb angle does not relate to quality of life measures.

14. F  Rigid bracing for vertebral compression fractures is superior to no brace in conservative management.

15. T  Greater trochanteric bursitis can cause radiation of pain down the lateral thigh to the knee joint, similar to that seen in lumbar radiculopathy.

16. T  For posterior lateral mass screw fixation of C1, the screws should angle medially for ideal trajectory.